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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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# RADIUM METABOLISM IN RATS, AND THE PRODUCTION OF OSTEOGENIC SARCOMA BY EXPERIMENTAL RADIUM POISONING*

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## INTRODUCTION

TWENTY to thirty years ago the internal administration of radium salts was a moderately popular but misguided therapeutic measure. In 1924 Blum[2] identified radium as the responsible agent in an occupational poisoning case resulting in osteomyelitis of the mandible and maxilla. The clinical and pathological studies of Martland and others[4,6,16] soon disclosed a number of cases of occupational radium poisoning acquired primarily in the radium dial painting industries during World War I. Other cases of fatal radium poisoning soon appeared, resulting from the oral or intravenous administration of radium, or other radioactive substances such as mesothorium.

With varying degrees of success, several clinicians have undertaken to relieve cases of chronic radium poisoning by treatment employing parathormone therapy,[1,12,13] or by a low calcium diet,[26] and based primarily on the close biochemical similarity between calcium and radium.

Clinically, cases of radium poisoning may be divided into acute and chronic types, with the usual continuum of intermediate cases. The acute cases result from the fixation in the skeleton of relatively large quantities of radium, and are characterized by a short and invariably fatal course accompanied by a marked secondary anemia, leukopenia, extensive hyperplasia of bone marrow, and pathological changes in the kidneys and other soft tissues. Rarefaction and spontaneous fractures of bone are common. In chronic cases, resulting from the fixation in the skeleton of relatively small quantities of radium, the course of the disease is much longer, lasting from five to fifteen or twenty years. There is often no deviation from a normal blood count, tissue abnormalities are much milder, and osteogenic sarcoma is often seen as a terminal condition.

Because of the interesting possibility that suitable clinical treatment may relieve some cases of chronic radium poisoning, clinical and experimental studies are of

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special interest. In recent years it has become possible to make accurate physical analyses on patients, whereby quantitative data on the radium burden, the radium metabolism and the radium excretion may be relied upon. A few representative cases have been published.[1] Unpublished data on a number of patients, seen by Dr. H. S. Martland of Newark and Dr. J. C. Aub of Boston, have served to emphasize the large biological variations between individuals in the radium dosage and the radium burden required to produce the usual clinical symptoms of chronic radium poisoning. In general, chronic radium poisoning is eventually seen in individuals containing from 1 to 10 micrograms of radium. Due to wide biological variations some patients containing only 2 micrograms of radium have been more quickly and more seriously affected than others containing as much as 20 micrograms of radium.

The clinical symptoms of chronic radium poisoning ordinarily appear only after a lapse of five to fifteen years from the time the radium entered the body. Thus in any individual patient the full course of the disease has seldom, if ever, been observed clinically. Some patients have been seen immediately after an accidental ingestion of radium, others shortly after the onset of the first clinical symptoms many years after radium was taken into the body, and still others have been seen only terminally. To assist in gaining a better clinical understanding of the full course of chronic radium poisoning it has seemed worth while to imitate the disease in experimental animals, where the time elapsed between the administration of radium and death might be compressed to one or two years. Previous studies of experimental radium poisoning in animals[15,20,21,23,27] have involved such large dosages that the animals imitated acute radium poisoning, usually exhibiting marked blood changes and never living long enough to develop sarcomas, except in the work of Sabin, Doan and Forkner,[23] who obtained osteogenic sarcomas in 2 out of 7 rabbits in eleven to nineteen months.

Accordingly, between 1936 and 1941 we have induced chronic radium poisoning in four series of male albino Wistar rats. Extensive quantitative observations of the metabolism of radium have been made in the first three series. The highlights of these observations and some comments on the pathological conditions induced are reported in the present paper. Primary osteogenic sarcoma is a terminal symptom in some of these experiments. The full course of the disease in these animals correlates well with both published and unpublished observations on patients seen for short periods at various stages of the long course which chronic radium poisoning runs in man. Pathological studies were emphasized in the fourth series of animals, which is being reported in a separate paper.[5] The osteogenic sarcomas induced in the fourth series of animals have been successfully transplanted by C. E. Dunlap and have now been carried through more than seven serial generations of rats. This should provide an interesting source of experimental material for laboratory studies of osteogenic sarcoma, especially with the use of artificially radioactive calcium, strontium, and other elements, when war-time activities allow a return to such investigations.

When these experiments were begun there was very little quantitative information relating to the minimum dosage required to produce injury in man. We therefore hoped that the rat experiments might be useful in estimating a tentative tolerance value for human beings. Tolerance data are obviously of importance to the United States Food and Drug Administration and to other agencies involved in the control of radium nostrums, and in the protection of personnel in industries using radioactive materials. The enormous expansion of the radium dial painting industry during the present war has given new urgency to the problem of determining a reasonable figure for the tolerance value in humans.

The very great difference which exists between species in resistance to toxic substances always introduces a profound un-

certainty in the extrapolation of any animal result to man. The tolerance values in animals may be interesting where there is an absolute lack of observations on man, but even a few measurements on man must be regarded as overwhelmingly more important in determining the tolerance dosage for man than the most elaborate experiments on animals.

Unpublished observations by Drs. J. C. Aub and R. D. Evans now include 7 human cases in which more than 0.02 μg. and less than 0.5 μg. of radium has been carried for some seven to twenty-five years without the appearance of any clinical symptoms of chronic radium poisoning. On the other hand, several unpublished cases seen by these workers, and others seen by Dr. H. S. Martland, have resulted fatally when the burden was between 0.5 and 2 μg. of radium. These observations have led to the tentative establishment[24] by a committee of the National Bureau of Standards of 0.1 μg. of radium fixed in the body as the tolerance value for humans. This figure replaces tolerance values of 10 μg. and 1.0 μg. recommended by individual observers[19] a number of years ago, before adequate physical methods were available for detecting smaller quantities of radium in living human beings. Whether or not the present tentative tolerance value of 0.1 μg. of radium is also optimistic when applied to a large group of individuals can be determined by accurate routine physical studies of the many hundreds of individuals who have entered the radium dial painting profession during the present war.

## ANIMAL LABORATORY PROCEDURES

*Series I.* The 11 male albino rats used in this series were obtained directly from the Wistar Institute, were fifty-five to sixty days old and 214 to 267 grams in weight at the start of the experimental period. They were separately housed in 12×6×6 inch galvanized wire cages, and fed a good stock diet[22] and glass-distilled water *ad libitum*. The cages rested on Glasbak dishes of such size that all food, urine and feces falling from above would be recovered.

Six of the animals were kept as controls. The remaining 5 received supplemental radium by medicine droppers, beginning November 2, 1936. The radium was diluted with physiological saline and glycerine so that 4 drops fed daily for twenty days would contain the desired quantity of radium. Glycerine was used to make the feeding more palatable. Drinking water was removed from the cages each evening and returned each morning after the thirsty rats had been given the supplemental feeding.

The droppings into the dishes below the cages were removed twice weekly, each collection being placed into a 16 oz. wide mouth glass-stoppered bottle, the dish was washed with 10 successive amounts of 1 M hydrochloric acid (saturated with barium chloride) and the dish returned to its place for the next collection. Thus any radium remaining on these dishes was carried into the subsequent collection. The collected samples were stoppered and sealed with wax to prevent the escape of radon generated by the radium in the sample. At the conclusion of the experiments the cages and trays were analyzed and found to have retained a negligible amount of radium.

The attendant feeding the rats wore rubber gloves which were washed with acid solution at the end of each day's feeding and these washings were collected. At the end of the feeding period the ampules, droppers and bottles used in feeding were placed in the jar containing the glove washings, and sealed. The radium in this jar represented that which had not been fed.

The radium used in this series was contained in 2 cc. ampules in the form of a halide. The ampules for animals No. 16212, 16213, 16214 contained radium as radium chloride in isotonic saline (U. S. Radium Corp.). The ampules for animals No. 16834 and 16835 contained radium as radium bromide in distilled water, with less than 3 per cent as much barium as radium (Luminous Processes, Inc.). Each ampule was analyzed for radium by the gamma-ray method before being opened. The amount of radium actually used in the experiments was determined by subtracting the radium content of the empty ampules, droppers, bottles and glove washings from the radium content of the ampules.

*Series II.* Six male white rats were obtained from Wistar Institute, were fifty-three to

FIG. 1. Roentgenogram showing osteogenic sarcoma in lumbar vertebra of rat No. 16212, at death.

sixty-five days old and weighed 233 to 250 grams at the start of the experimental period. The procedure was substantially the same as in Series I. However, the experiment was started seventeen months later, June 10, 1938, and the radium element was fed daily for ten days to 3 rats, as a bromide compound (Luminous Processes, Inc.) in isotonic saline and glycerine, the remaining 3 animals being kept as controls. The actual quantities fed were estimated by the same procedure. Each day during the radium administration the excreta were collected and subsequently analyzed for radium content.

*Series III.* Concurrently (June 15, 1938) with Series II, 6 Wistar rats, fifty-three to sixty-five days old and weighing 215 to 244 grams were subjects in an experiment in which 3 of the experimental rats were given the radium intradermally at the midline of the abdomen. A mixture of 5 cc. distilled water, 181 micrograms of radium as bromide, 80 milligrams of barium chloride and 0.94 cc. of physiological saline solution was used for the injection. Each animal received five injections of 0.3 cc. each, at two-day intervals, from this solution. As in the other series, the actual amount of radium used was calculated from the results of measurements of the radium remaining in the containers after injections had been made.

*Series IV.* Thirteen male Wistar Institute rats, twenty-one weeks old, were fed three drops (0.13 cc.) per day for twenty days, of a solution containing 1,500 μg. of radium (supplied as crystalline bromide by the S. W. Shattuck Co., Denver) in 13 cc. of glycerine, and 26 cc. of 0.9 per cent sodium chloride. Correcting for the measured radium content of the feeding bottle and dropper at the end of the experiment, each animal in this series received 100 μg. of radium element. The feedings were begun on January 13, 1941. In about a year 9 of these animals developed osteogenic sarcomas, reported in detail elsewhere.[5]

The laboratory data on Series I, II, and III are presented in Table I. Most of the animals died during the experimental period but in several cases they were killed. The general procedure used in preparing tissues for radium assay was as follows: Thoracic and abdominal cavities were opened, and the lungs, kidneys, liver, heart, spleen, testes and viscera of each animal were each placed in a separate bottle. The muscle tissue and skin were removed as completely as possible and placed in another bottle. Then the skull, spine and tail, ribs, pelvic girdle, fore legs and scapula, and hind legs were each placed in bottles. The weighed contents of each bottle were digested with nitric acid on a steam bath until the acid solution was relatively clear. This nitric acid was prepared from Grasselli c.p. reagent nitric acid by redistillation in glass, retaining only the center 90 per cent cut. Control tests on the prepared acid showed it to be free from radium and its decay products.

After digestion of the samples, the bottles were stoppered and sealed with wax. This complete separation of tissues and organs was not made in preparing the first animals to die in Series I and in several instances samples were taken for pathological examination and not analyzed for radium content.

## PATHOLOGICAL FINDINGS

*Series I.* Rat No. 16212 developed an osteogenic sarcoma in the upper lumbar vertebra (Fig. 1). He died 438 days after

the first radium feeding. On postmortem he showed marked cystitis, enlarged kidney showing albuminous degeneration of the proximal convoluted tubules. Some regions of the bone showed distortion of the normal architecture with occasional islands of cartilage. In other areas the marrow was replaced by highly vascularized fibrous tissue with fibroblasts varying in size and shape and rarely showing mitotic figures. The spleen showed increased fibrosis of

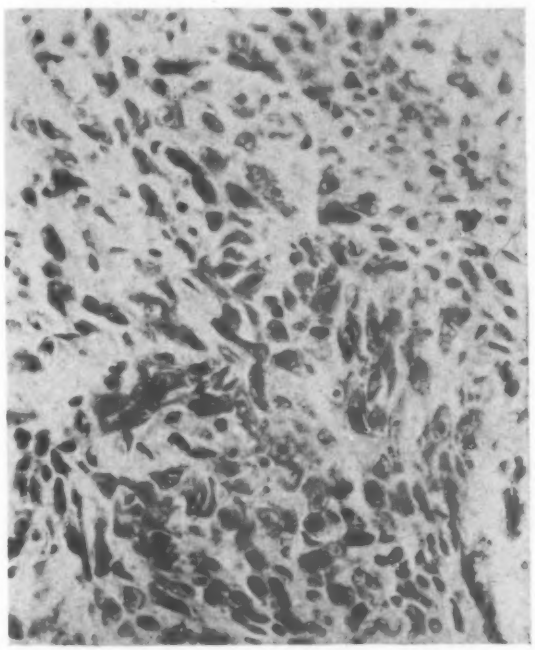

Fig. 2. Rat No. 16213. Lung metastasis. Hematoxylin-eosin. (×400)

trabeculae in the reticulo-endothelial cells; some arterioles showed moderate hyaline thickening. The heart and liver were negative. Death was probably due to ascending infection of the urinary tract. Microscopic section showed osteogenic sarcoma. Tumor of the spine contained 39.5 units of phosphatase per gram, by the method of Franseen and McLean.[14]

Rat No. 16213 was killed 537 days after first radium feeding. At postmortem there was a small abscess near an old fracture of the right tibia, a lung abscess about 7 mm. in diameter, and several metastases (Fig. 2)

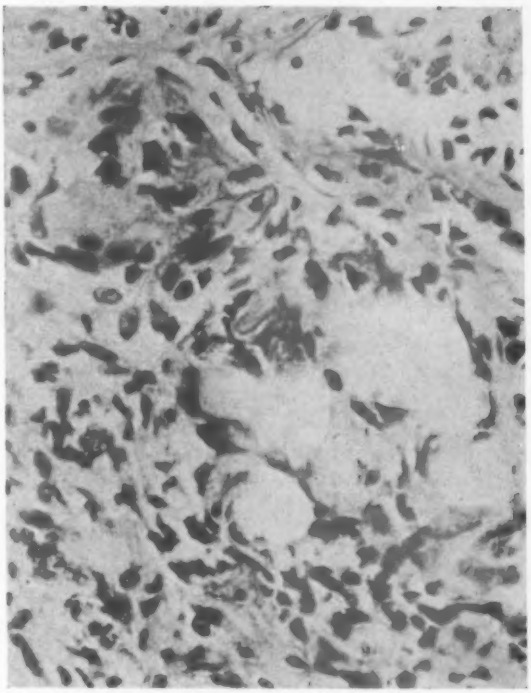

Fig. 3. Rat No. 16213. Section of the original tumor (osteogenic sarcoma) in the right femur. Hematoxylin-eosin. (×400)

in the lungs, each about 3 mm. in diameter. A tumor, 1 cm. in diameter, occupied the upper end of the right femur (Fig. 3) and

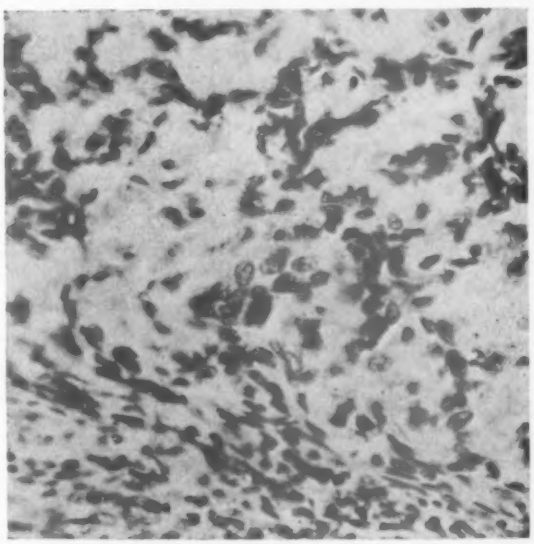

Fig. 4. Rat No. 16213. Metastasis in spleen, with uninvolved splenic tissue in lower left corner. Hematoxylin-eosin. (×400)

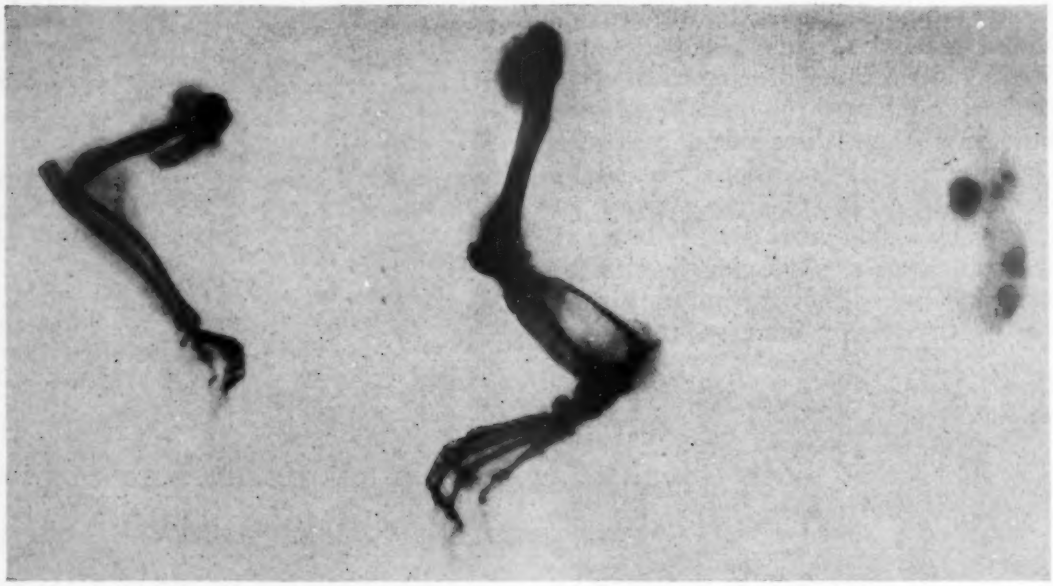

FIG. 5. Roentgenograms of sarcomatous left arm and right leg, and of calcified spleen, all from rat No. 16213, at the time of death.

contained encapsulated bone spicules. A second tumor was present at the upper end of the right humerus which was softer and more granular than the femur tumor, but the same size. The spleen was largely replaced by five discrete metastases (see Fig. 4, also roentgenogram, Fig. 5); the largest was 10×5×6 mm. and perhaps was composed of two foci. Each was stony hard, and had white bone-like centers. The liver and other abdominal organs had no metastases. The tumor from the humerus (see roentgenogram Fig. 5) showed irregular masses of fibroblasts varying somewhat in size, with numerous tumor giant cells and infrequent mitoses. There was considerable collagen and a slight deposition of osteoid, resembling a poorly differentiated sarcoma, though occasionally there were foci of well formed trabecular osteoid with a suggestion of calcification. The tumor from the femur (see roentgenogram, Fig. 5) was much less cellular, with relatively plump fibroblastic cells peripherally; and with rather sparse more or less elongated, fibroblastic cells, and rare mitoses. Peripherally there was a slight amount of intercellular collagen and virtually no osteoid. Centrally there was a moderate amount of osteoid and some fairly dense, partially hyalinized collagen, appearing like a moderately well differentiated osteogenic sarcoma. The lung contained several small foci of well formed osteoid, with some calcification, the surrounding cells being irregular in size and shape with rather dense, pyknotic nuclei and occasionally showing mitotic figures. Not only did the tumor invade the lung parenchyma but it grew freely within some of the great vessels as well. The adjacent lung parenchyma showed moderately intense inflammatory reaction probably due to secondary infection. The spleen showed nodules of tumor very similar to that present in the femur, with much osteoid and hyaline, fibrous tissue; a moderate number of irregular polyhedral tumor cells was scattered throughout the substance of the tumor. Here and there mononuclear cells filled with hemosiderin were present. The kidney showed albuminous degeneration of the convoluted tubules. The glomerular tufts were somewhat edematous, otherwise not remarkable. The phosphatase content of the femur tumor was 42.7 units per gram

while that of the metastases of the spleen was 55.0 units per gram.

Rat No. 16214 died 558 days after the first feeding of radium. During the last eighty days of this period he lost considerable weight. Roentgenograms taken at death showed evidence of osteogenic sarcoma in the pelvic region of the spine, but this was not confirmed by pathological examination. The lungs were filled with multiple small abscesses, confirmed by frozen sections.

Rat No. 16834 died 377 days after first radium feeding. He showed a mass in the pelvis by roentgen examination (Fig. 6) and a tumor at autopsy. Death came early in a weekend and the tissues were too necrotic for satisfactory study. However, tumor was represented by irregular strands of bone and osteoid tissue (25×11×10 mm.) presenting various degrees of calcification. The irregularity in architecture and general distortion, the relation of the bone and osteoid trabeculae to the necrotic soft tissues warrant a diagnosis of osteogenic sarcoma. Pelvic tumor contained 98.6 units of phosphatase per gram and 0.037 microgram of radium per gram, and weighed about 1.5 grams.

Rat No. 16835 died 383 days after first feeding of radium. Before pathological study, the right leg was removed for chemical analysis (see Table III). The lung was irregularly infiltrated by clusters of large

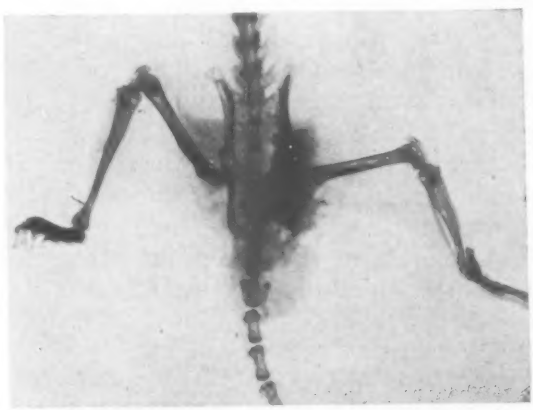

Fig. 6. Roentgenogram showing sarcoma in the pelvis of rat No. 16834, at death.

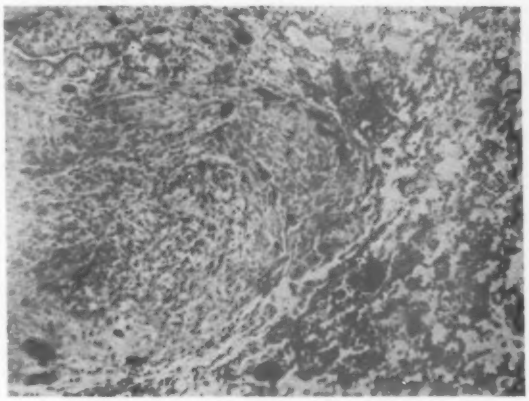

Fig. 7. Rat No. 16835. Low power view of nodule in lung invading normal lung tissue. Hematoxylin-eosin. (×60)

fibroblastic cells arranged in somewhat irregular strands, invading and destroying normal lung parenchyma (Fig. 7). There was moderate variation in the cytologic picture, some tumor giant cells being present. Mitotic figures were moderately frequent. There was a slight amount of collagenous intracellular substance present. The remainder of the lung showed some fibrosis and infiltration with polymorphonuclear leukocytes, lymphocytes, and mononuclear leukocytes. There was some purulent exudate in the bronchi. Rare vessels showed thromboses. The section of bone available for study appeared within normal limits except for irregularity of cartilage in the region of the epiphyseal line, and moderate variation in the contour of adjacent bone trabeculae. There was slight fibrosis and paucity of hematopoietic cells in the marrow adjacent to the epiphyseal line. The liver showed a few foci of trabeculation and rarefaction of the cell columns about the central venules. The kidney showed considerable postmortem change with varying albuminous degeneration of the proximal convoluted tubules, and the glomeruli were not remarkable. The testes were not unusual, but the spleen showed some diffuse fibrosis.

*Series II.* Rats No. 20950, 20951, and 20952 died 455 to 462 days after the first feeding of radium. The apparent cause of

death was pneumonia. Roentgenograms taken during the test period and after death showed no evidence of osteogenic sarcoma or of tumors.

*Series III.* Rat No. 20953 died 224 days after the first injection of radium. He had lost 35 grams in weight during the last sixty-one days of life. Death may have been due to bronchopneumonia. Pyelonephritis was noted on microscopic examination, but the bone was negative and no tumors were found.

Rat No. 20954 died 302 days after the first radium injection. He had lost 105 grams in weight during the last 139 days of life. Microscopic examination showed tubular nephritis, eburnation of the bone with slight fibrosis, and no tumors.

Rat No. 20955 was killed 143 days after the first radium injection. He had lost 28 grams in weight during the last forty-seven days of life. At the end there developed complete paralysis of both hind legs but no cause for this could be found on postmortem examination, though it may have resulted from the hydronephrosis which was found. No evidence of tumor was noted.

*Series IV.* Of the 13 animals in this series, 9 developed primary osteogenic sarcomas in time intervals of 253 to 426 days after the first radium feeding. The average induction time of the tumors was 365 days. The primary growths were in the vertebrae in 7 rats and in the pelvic bones in two. Complete pathological findings have been described elsewhere.[5]

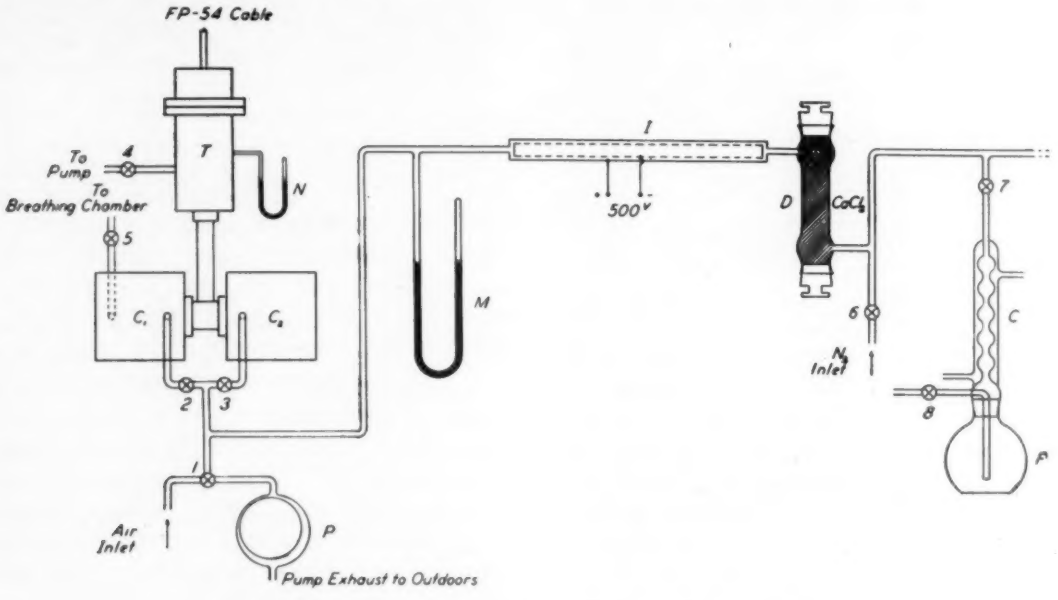


FIG. 8. Schematic diagram of the apparatus for measuring the radium content of tissues, bones, and excreta.

*Controls.* The control animals for each of the four series were given the same environment and dietary and differed only in that they received no radium. Their weight increased throughout the test periods. After the last animal in each group had died, the controls for that group were roentgenographed. None showed evidences of sarcoma or tumors. Since they appeared to be normal, these animals were used in successful attempts to transplant the osteogenic sarcomas which had appeared in the test animals.

### MEASUREMENT OF RADIUM IN EXCRETA AND IN POSTMORTEM MATERIALS

The balanced double ionization chamber method,[7] modified primarily by substituting a vacuum tube electrometer[18] for the

string electrometer, is used for measuring the radon accumulated in and released from solutions of bones, tissues, and excreta. The radium content of the sample is then obtained by the usual elementary calculation.

A schematic diagram of the complete radon measuring apparatus is shown in Figure 8. Stopcocks *2* and *3* allow independent pumping of the two balanced ionization chambers, $C_1$ and $C_2$. Each ionization chamber is about 13 cm. in length and diameter, has a volume of 1.89 liters, has brass walls and a 1 mm. brass center wire, has tapered pressed-amber insulators with guard rings, and contains a renewable cartridge of $P_2O_5$ for keeping the insulation thoroughly dry. The electrometer tube chamber $T$ can be evacuated through stopcock *4*, the manometer $N$ serving only as a rough indicator of the pressure.

In operation, one chamber, usually $C_1$, is pumped out, the pressure being read by a mercury manometer at $M$. The solution containing the radium and radon is in flask $F$ and is boiled for twenty minutes, nitrogen meanwhile bubbling through the solution after entering at stopcock *8*. The radon and nitrogen pass through the water-cooled condenser $C$, the $CaCl_2$ drying tube $D$, and the ion trap $I$, into $C_1$, the rate of flow being such that the pressure in $C_1$ reaches one atmosphere at the end of the twenty-minute period. Stopcocks *2*, *7*, and *8* are then shut off, the amplifier attached to the *FP-54* cable is balanced, and the photographic record of the amplified ionization current is begun. Using a grid resistor of 94,000 megohms the sensitivity was $8.25 \times 10^{-9}$ curies per volt change in grid voltage.

Following each analysis, the ionization chambers are pumped out and filled with nitrogen which enters at *6*. Four or five flushings with nitrogen are sufficient to clean the chambers of all residual radon.

### BREATH MEASUREMENTS ON THE LIVING RATS

At various times during the experiments all of the rats were measured for the radon content of their exhaled breath. For this purpose an ionization chamber ($C$ in Fig. 9) was built with a removable extension ($R$) in which the rat is housed. At the junction are two polished plates ($P_1$, $P_2$) with two 1 inch holes cut in each. These act as a valve, enabling the ionization chamber to

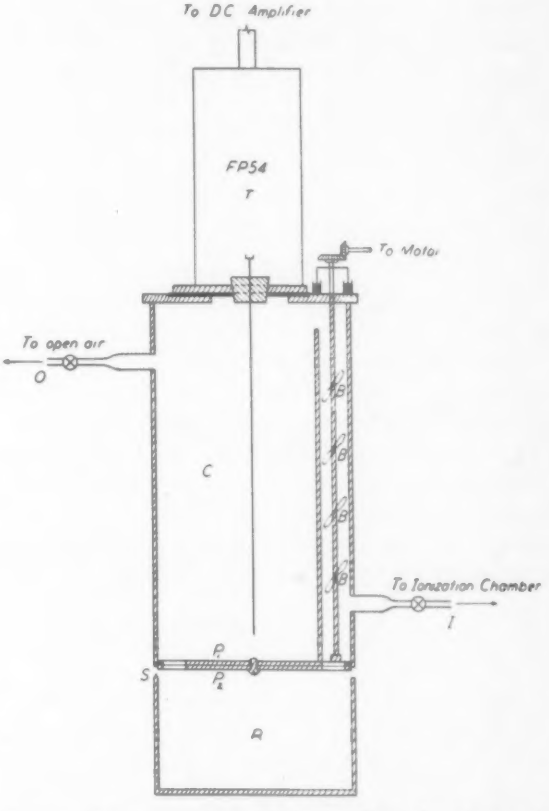


Fig. 9. Cross-section of the ionization chamber and rat breathing chamber for measuring the rate at which the rats exhaled radon.

be isolated from the rat breathing chamber ($R$) by rotating the rat chamber 90°.

Each rat is kept in the chamber for five or ten minutes and then the chamber is sealed off and the rat removed. While the rat is in the chamber a mercury sealed stirrer ($B$) mounted near the side of the ionization chamber circulates the radon and air throughout the chambers $C$ and $R$. The radon exhaled by the rat is calculated from the radon measured in $C$ (volume = 5,590 cc.) by correcting for the volume of the rat chamber (1,380 cc.) minus the volume of the rat (assuming specific gravity equals

1.0). Thus the total radon $Rn$ is given by

$$Rn = Rn'(6970 - m)/5590$$

where $m$ is the weight of the rat, and $Rn'$ is the amount of radon measured in chamber $C$. The radium $Ra$ producing this radon is given by

$$Ra = Rn/\lambda T$$

where $\lambda = 2.1 \times 10^{-6}$ sec$^{-1}$ is the decay constant of radon, and $T$ is the number of seconds the rat breathes in chamber $R$.

The radon in $C$ is measured by an $FP-54$ vacuum tube electrometer,[18] whose sensitivity is such that $7.67 \times 10^{-9}$ curies of radon in $C$ produces a change in grid potential of one volt. Calibration is made by flowing radon produced in a standard radium solution through $C$ and through $C_1$ of Figure 8 in series at atmospheric pressure. By measuring the radon in $C_1$, and the volume of both $C_1$ and $C$, the radon introduced in $C$ can be determined accurately. The chamber $C_1$, which can be evacuated, is calibrated separately in the usual way,[7] using a dilute standard radium solution obtained from the National Bureau of Standards.

## GAMMA-RAY MEASUREMENTS ON LIVING RATS

Most of the rats were measured with a Geiger-Müller counter for gamma-ray activity, by comparison with a known standard at the same distance from the counter tube. The rat was housed in a small cage $6 \times 3 \times 3$ inches in size. The bottom, sides, and ends were then fitted with pieces of corrugated cardboard to prevent the rat from changing his position. Guides along the top of the cage held the counter in a fixed position relative to the rat. The data were recorded with a counting rate meter.[9]

It was necessary to correct these data for absorption of the gamma rays in the rat. The detailed method developed for use on human beings[8] was modified by including higher algebraic terms in the expansion leading to equation (9) of that paper in order to account for the larger ratio between animal thickness and the separation between animal and counter. It was found that the rats had a mean effective thickness of 6 cm., that the mean absorption coefficient for radium series gamma rays was 0.073 cm.$^{-1}$ in the bones and tissues of the rat, and that the inverse square law becomes an inverse 1.4 power law when the counter is parallel to and 9 cm. from the long axis of the rat, and an inverse 1.8 power law at 20 cm. This deviation from the inverse square law is to be expected because neither the counter nor the animal represents mathematical points, but have dimensions comparable to the distance between them.

The results of the radium measurements on all three series of rats are given in Table 1.

## EXCRETION AND RETENTION OF RADIUM

Radium analyses were made on each individual sample of mixed feces and urine, representing biweekly collections from Series I, and daily collections from Series II and III during the feeding or injection period and for a short time thereafter. Collections containing more than about 0.2 μg. of radium were simply sealed and stored for a month to permit the establishment of radioactive equilibrium. Then their gamma-ray activity was compared with that of standard radium solutions, using screen cathode gamma-ray counters[11] and a counting rate meter. Corrections were applied for the internal absorption of the radium C gamma rays within the sample.* Collections containing less than about 0.2 μg. of radium were digested in redistilled nitric acid and their radium content determined by measurements of their rate of production of radon.

Measurements of the actual radium content of the living rats were made using the techniques described in the previous section, the total radium content being the sum of the amounts of radium required to produce the radon in the exhaled breath

* The method of Patterson, Walsh, and Higgins[17] was generalized to include correction terms for the decrease of gamma-ray intensity with distance, for each volume element in the cylindrical source.

TABLE I

SUMMARY OF THE RADIUM MEASUREMENTS

| | Series I—Oral | | | | | Series II—Oral | | | Series III—Injected | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Animal Number | 16212 | 16213 | 16214 | 16834 | 16835 | 20950 | 20951 | 20952 | 20953 | 20954 | 20955 |
| Attempted dosage, μg. Ra | 50 | 50 | 25 | 100 | 100 | 50 | 50 | 50 | 50 | 50 | 50 |
| Probable dosage, μg. Ra | 22 | 28 | 10 | 62 | 70 | 40 | 26 | 24 | 6 | 4 | 3 |
| Weight in grams. Initial | 231 | 245 | 233 | 267 | 264 | 250 | 233 | 242 | 240 | 215 | 221 |
| Maximum | 344 | 320 | 388 | 386 | 386 | 358 | 340 | 354 | 330 | 315 | 342 |
| Final | 233 | 319 | 300 | 386 | 393 | 332 | 304 | 350 | 295 | 210 | 314 |
| Days survival after beginning Ra | 438 | 537 | 558 | 377 | 383 | 462 | 455 | 462 | 224 | 302 | 143 |
| Suggested cause of death | Nephrosis | Killed | Pneumonia | Unknown | Unknown | Pneumonia | Pneumonia | Pneumonia | Bronchopneumonia | Nephritis | Killed |
| Developed osteogenic sarcoma | Yes | Yes | Probable | Yes | Probable | No | No | No | No | No | No |
| *Radium measurements on living rats* | | | | | | | | | | | |
| Days after beginning radium | 381 | 427 | 394 | 245 | 309 | 170 | 175 | 178 | 190 | 193 | 195 |
| μg. Ra as exhaled breath Rn | 0.91 | 0.71 | 0.27 | 4.4 | 3.0 | 0.36 | 0.62 | 0.68 | 3.2 | 1.7 | 1.3 |
| μg. Ra as gamma rays from body | 0.12 | 0.13 | 0.04 | 0.46 | 0.79 | 0.07 | 0.10 | 0.12 | 1.1 | 0.8 | 0.8 |
| μg. Ra total in living body | 1.03 | 0.84 | 0.31 | 4.86 | 3.8 | 0.43 | 0.72 | 0.80 | 4.3 | 2.5 | 2.1 |
| Percentage body Ra shown as breath Rn | 88 | 84 | 87 | 90 | 79 | 84 | 86 | 85 | 74 | 68 | 62 |
| *Radium measurements postmortem* ($10^{-9}$ gm. Ra/gm. wet weight | | | | | | | | | | | |
| Kidney | 0.0075 | — | 0.053 | 0.023 | 0.046 | 0.000 | 0.018 | 0.075 | 0.31 | 0.25 | 0.08 |
| Spleen | 0.004 | — | — | 0.006 | 0.043 | — | — | 0.11 | 0.027 | 2.7 | 0.15 |
| Liver | 0.0008 | — | 0.0005 | 0.015 | 0.017 | 0.015 | 0.0046 | 0.009 | 0.26 | 0.12 | 0.010 |
| Intestines | — | — | 0.25 | — | — | 0.0054 | 0.060 | 0.030 | — | — | — |
| Heart | 0.02 | — | 0.004 | 0.015 | 0.15 | 0.002 | 0.018 | 0.005 | 0.0006 | 0.12 | 0.0005 |
| Lungs | 0.69 | — | 0.10 | 1.8 | 1.1 | 0.12 | 0.087 | 3.7 | 0.11 | 0.47 | 0.38 |
| Testes | — | — | — | — | — | 0.031 | — | 0.009 | 0.33 | — | 0.004 |
| Muscle, skin and fur | 0.005‡ | — | — | 0.006‡ | 0.09‡ | 0.31 | 0.68 | 0.50 | — | 20 | — |
| Legs | — | — | 13 | — | — | 48 | 58 | 49 | 83 | 70 | — |
| Arms and scapula | — | — | 14* | — | — | 45 | 35 | 50 | 86 | 80 | — |
| Spine including tail | — | — | 24† | — | — | 26 | 34 | 30 | 54 | 50 | — |
| Pelvis | — | — | — | — | — | — | 47 | 46 | 73 | 81 | — |
| Skull and teeth | — | — | 32 | — | — | 36 | 51 | 60 | 62 | 86 | — |
| Ribs | — | — | — | — | — | 24 | 17 | 45 | 94 | 78 | — |
| Entire skeleton | ~90 | ~60 | ~25 | ~400 | ~400 | 34 | 42 | 43 | 79 | 68 | — |
| ($10^{-9}$ gm. Ra in total tissue) | | | | | | | | | | | |
| Kidney | 0.022 | 0.030 | 0.21 | 0.061 | 0.12 | 0.0005 | 0.022 | 0.15 | 0.57 | 0.063 | 0.046 |
| Spleen | 0.001 | 0.043 | — | 0.001 | 0.029 | — | — | 0.022 | 0.073 | 0.26 | 0.014 |
| Liver | 0.003 | — | 0.002 | 0.043 | 0.12 | 0.097 | 0.031 | 0.055 | 2.2 | 0.46 | 0.066 |
| Intestines | 1.3 | 0.58 | 4.9 | 2.2 | 2.6 | 0.070 | 0.74 | 0.36 | — | — | — |
| Heart | 0.014 | 0.005 | 0.008 | 0.015 | 0.33 | 0.004 | 0.036 | 0.010 | 0.0009 | 0.089 | 0.001 |
| Lungs | 1.9 | 1.8 | 0.19 | 4.2 | 3.0 | 0.25 | 0.18 | 7.20 | 0.40 | 0.45 | 0.058 |
| Testes | — | 0.47 | — | — | 0.07 | 0.017 | — | 0.040 | 0.29 | — | 0.015 |
| Muscle, skin and fur | 0.013‡ | 15.7 | — | 0.012‡ | 0.23‡ | 33.6 | 62.7 | 59.9 | 3400 | 2100 | — |
| Legs | — | 108 | 16 | — | — | 76 | 117 | 113 | 333 | 171 | — |
| Arms and scapula | — | 66 | 21 | — | — | 40 | 31 | 45 | 175 | 75 | — |
| Spine, including tail | — | 282 | 146† | — | — | 102 | 186 | 180 | 320 | 265 | — |
| Pelvis | — | 61 | — | — | — | — | 47 | 55 | 118 | 131 | — |
| Skull and teeth | — | 127 | 58* | — | — | 123 | 158 | 191 | 424 | 248 | — |
| Ribs | — | 42 | — | — | — | 12 | 8 | 27 | 108 | 47 | — |
| Entire skeleton | 918 | 632 | 241 | 3970 | 3790 | 353 | 547 | 611 | 1478 | 937 | — |
| Total Ra in all tissues, μg | ~1.0 | ~0.67 | ~0.28 | ~4.4 | ~4.2 | 0.42§ | 0.61 | 0.68 | 4.9 | 3.0 | ~2.1 |
| Total Ra excreted during life, μg. | 21.0 | 27.0 | 10.0 | 58.0 | 66.0 | 40.0 | 25.0 | 23.0 | 1.5 | 0.9 | 0.5 |
| Total Ra, excreta and tissues, μg. | 22.0 | 27.7 | 10.3 | 62.4 | 70.2 | 40.4 | 25.6 | 23.7 | 6.4 | 3.9 | ~2.6 |
| Percentage Ra retention at death | 4.5 | 2.4 | 2.7 | 7.0 | 6.0 | 1.0 | 2.4 | 2.9 | 77 | 77 | ~80 |

* Lower jaw removed. † Ribs, spine, tail, scapula and pelvis. ‡ Leg muscle only. § Including 0.03 μg. estimated for pelvis.

and to produce the gamma rays emitted from the rats' bodies. Radium analyses were also made postmortem, by the radon method, on the principal organs and tissues, and on the skeletons.

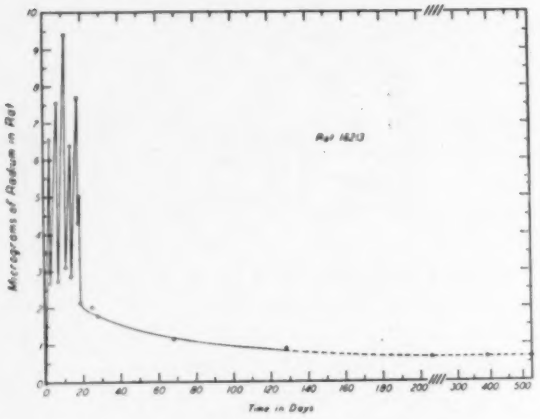


Fig. 10. Retention of radium, in micrograms, in rat No. 16213 which was fed a total of 28 micrograms of radium in twenty daily doses. The animal retained 2.8 per cent of the dose at the time of death, 537 days after the beginning of the radium feeding. Osteogenic sarcoma was demonstrated (Fig. 5).

Originally, the actual amount of radium administered to each animal was estimated by deducting from the measured strength of the radium preparations the amount of radium remaining on the glassware, gloves etc., used in administering the dosage. Subsequently, this dosage estimate was compared with the sum of the total body content at death and the total excreta of each animal. The agreement was poor, in some cases as much as 40 per cent of the originally estimated dosage being unaccounted for in the excreta and body of some individual animals. Therefore in Table 1, and in the graphs of the dosage and excretion of the individual animals, we have chosen the sum of the body radium at death and the total excretion during life as the best evaluation of the actual dosage for each individual animal.

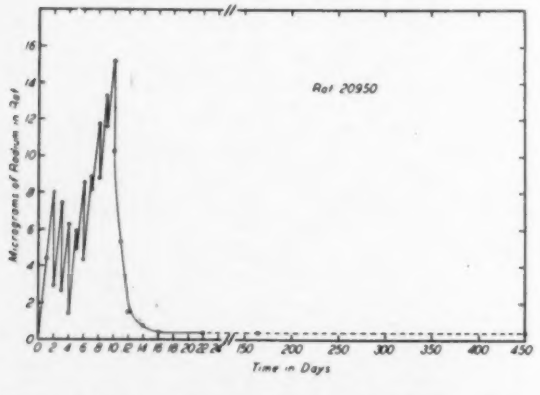


Fig. 11. Retention of radium in micrograms, in rat No. 20950, which was fed a total of 40 micrograms of radium in ten daily doses. The animal died of pneumonia 462 days later, having retained only 1.0 per cent of the radium fed. See Table 1. Note the unusually rapid excretion of radium during and immediately following the administration of the radium.

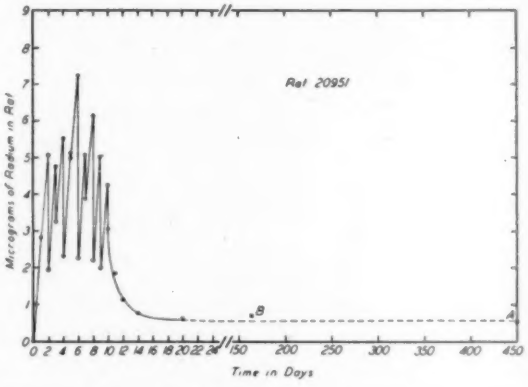


Fig. 12. Retention of radium, in micrograms, in rat No. 20951, fed a total of 26 micrograms of radium, and retaining 2.4 per cent of it at death. Point *A* is radium found in bones and tissues postmortem; point *B* is radium in living animal determined from the sum of body gamma rays and exhaled breath radon.

In Series II and III, the entire skeletal musculature, plus the skin and fur, was analyzed for radium, but this was not done in Series I. The results from Series II indicate that after oral administration about 10 per cent of the total radium is found in the muscle, skin and fur sample. An unknown fraction of this radium may be external. In estimating the total dosage and retention for Series I, we have added 10 per cent of the measured skeletal radium content, to represent the radium content of the total muscle, skin and fur.

The excretion of ingested radium in rep-

resentative animals from Series I and II is shown in Figures 10, 11, and 12. The solid portion shows the increasing radium content resulting from the administered dosages, determined as described above, and the loss of radium by excretion in the feces and urine.

The rapid initial excretion of ingested radium is evident. Within four days from the last administration of radium, 92 to 96 per cent of the total radium administered has been excreted. As in the case of humans (ref. 1; Case R.L.) this initially rapid fractional rate of excretion declines rapidly. A seven day collection of excreta from each animal in Series II was made 120 days after the conclusion of the feeding. These collections contained 0.016, 0.017, and 0.022 μg. of radium for animals No. 20950, No. 20951, and No. 20952 respectively. This corresponds to a daily elimination rate of 0.6 per cent, 0.3 per cent, and 0.4 per cent, respectively, of the body content as measured (Table I, Fig. 11 and 12) on the live animal. The higher fractional excretion rate in animal No. 20950 than in the other two animals was consistent with his smaller fractional retention of radium (see Fig. 11 and 12).

A few radium measurements were made during the lifetime of 4 of the 13 animals (No. 25630, No. 25631, No. 25632, No. 25633) of Series IV for body gamma rays, exhaled breath radon, and rate of radium excretion. These observations are summarized in Table II. All 4 animals died of osteogenic sarcoma and have been described pathologically in another place.[5] About 110 days after beginning the radium feeding the radium excretion rate for 2 animals was about 0.15 per cent per day, while the average excretion rate over the last seven months of life was 0.035 per cent per day. The 4 animals tested showed an average total radium retention at death of 2.2 μg., or 2.2 per cent of the amount fed.

TABLE II

SUMMARY OF THE RADIUM MEASUREMENTS ON SERIES IV

| Animal Number | No. 25630 | No. 25631 | | No. 25632 | | No. 25633 |
|---|---|---|---|---|---|---|
| Total radium fed, μg. | 100 | 100 | | 100 | | 100 |
| Days survival after beginning Ra | 253 | 318 | | 398 | | 398 |
| Developed oesteogenic sarcoma | Yes | Yes | | Yes | | Yes |
| *Radium Measurements* | | | | | | |
| Days after beginning Ra | 110 | 113 | 309 | 106 | 323 | 320 |
| μg. Ra as exhaled breath Rn | 3.12 | 1.53 | 1.42 | 1.85 | 1.72 | 1.23 |
| μg. Ra as gamma rays from body | 0.45 | 0.38 | | 0.27 | | |
| μg. Ra total in living body | 3.57 | 1.91 | ca 1.97 | 2.12 | ca 1.97 | ca 1.45 |
| Percentage body Ra shown as breath Rn | 87 | 80 | | 87 | | |
| μg. Ra excreted per day | 0.0050 | 0.0036 | | | | |
| Percentage Ra excreted per day | 0.14 | 0.19 | | | | |
| Percentage average daily excretion, 100 to 300 days | | 0.034 | | 0.034 | | |

Thomas and Bruner[27] found an average radium excretion rate of 0.09 per cent per day near the end of life in 2 rats which had received radium by subcutaneous injection.

Aub, Evans, Gallagher and Tibbetts[1] studied 1 patient who accidentally inhaled a small quantity of radium. They found an average daily excretion rate of about 2 per cent of the radium contained in the body four weeks after the accident, when the patient still contained about 0.8 microgram of radium. Seven weeks after the accident the patient contained 0.6 microgram of radium, and excreted about 1 per cent per day, while still on a normal high calcium diet. Medication was then instituted to maintain as high a rate of radium excretion as possible, and in the three weeks (from the ninth to twelfth week after the accident) the average excretion rate was 0.7 per cent per day. Six months later the patient was re-examined and found to have retained about 0.3 microgram of radium, of which 0.1 per cent was being excreted daily.

Studies on a number of chronic human cases have shown an average daily fractional excretion rate of about 0.005 per cent per day,[1,8,25] after radium has been in the body for several years.

In man, about 45 per cent of the radon produced by radium in the skeleton is exhaled, although this percentage may vary widely in exceptional cases. The remainder of the radon decays within the body into a series of solid radioactive products, one of which, radium C, emits strong gamma rays. Thus about 55 per cent of the body radium in man is usually exhibited as body gamma rays.

In the rats, the percentage of radon exhaled is much higher, as would be expected from their higher metabolic rate and their smaller size which allows for the more rapid transport of radon from the bones to the lungs. Both Series I and II (as well as 3 of the animals in Series IV) showed an average of 85 per cent of the body radium exhibited during life as radon in the exhaled breath, only the remaining 15 per cent giving rise to gamma rays from the body.

In a series of human beings who drank known quantities of a radium nostrum, from 0.1 to 10 per cent of the radium ingested was fixed chronically in the skeleton.[10] This fractional retention appears to increase with increasing dosage, and also to be dependent on the dietary calcium balance at the time of ingestion. An adequate calcium intake, prior to radium ingestion, probably minimizes the fixation of radium in the bones because of the close biochemical similarity between radium and calcium. In the animals studied, the terminal fractional retention after oral ingestion (Series I, II and IV) varies between 1 and 7 per cent, and may indicate an increase with increasing dosage.

At postmortem, the organs contain less than 1 per cent as much radium per gram as is found in the skeleton. The muscle, skin, and fur samples of Series II contained about 10 per cent as much radium as the skeleton. However, the low radium content of the leg muscle samples in Series I suggests that skeletal muscle also has a very low radium content. The possibility that the skin and fur were contaminated by radium from excreta cannot be excluded in our measurements on Series II.

Of the organs studied, the lung generally has the greatest and the heart the least concentration of radium per gram of tissue (Table 1). On the wet weight basis used throughout, the bones usually show at least a hundred times the radium concentration of the richest soft tissue. There is no remarkable variation in radium concentration from one bone to another, although the spine and ribs appear to exhibit the lowest concentration of radium per gram of bone. However, if comparisons on a dry weight basis were possible, the relative concentrations might be altered or even reversed because of the small amounts of cortical bone in the spine.

The distribution of total radium in the skeleton placed about 65 per cent in the axial system of skull and spine, some 7 per

cent in the fore quarters (scapula, arms, and hands), and about 28 per cent in the hind quarters (pelvis, legs, and feet).

In Series III, radium was administered by intradermal injection at the midline of the abdomen, but only about 10 per cent of the radium entered the animals. The remainder was found in the vials and syringe where it was apparently adsorbed by the glass in spite of the excess of barium chloride present in the neutral solution, which was prepared as described in the section on Animal Laboratory Procedures.

measurements on the live animals showed that there was a concentration of the radium at the site of injection even six months after the injections were made, and the high concentration of radium found in the skin of these animals at postmortem confirmed this. It is apparent, therefore, that the higher excretion rate in the injected series is due to the normal excretion of the radium which had entered the body upon injection and was first deposited in the tissues, plus an excretion of small amounts of radium which had been held

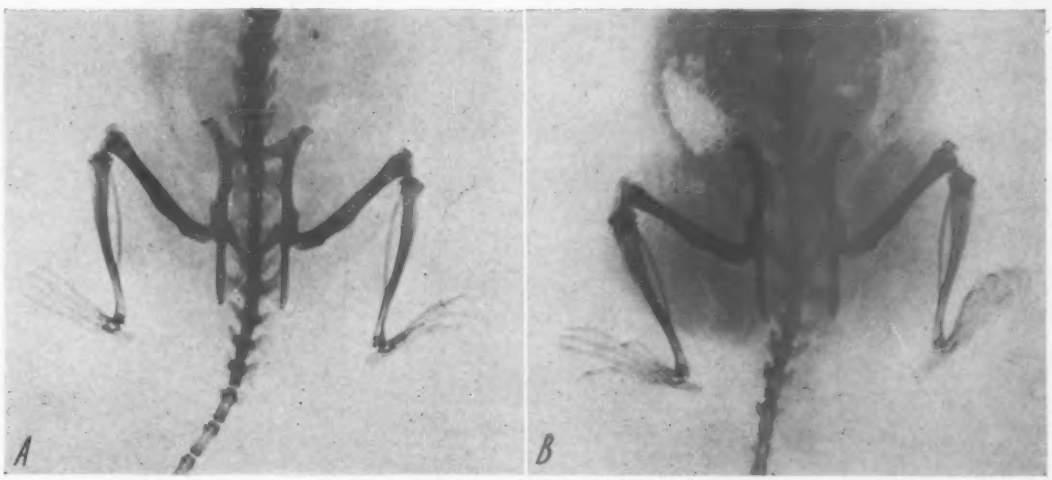


FIG. 13. *A*, roentgenogram of hind quarters of control rat No. 16833. *B*, roentgenogram of hind quarters of rat No. 16835. Both roentgenograms were taken 289 days after first feeding of radium to rat No. 16835. Note intense calcification in metaphysis of tibia and femur of radium-fed rat.

The initial absorption following intradermal injection was slow, as shown by an initially low radium excretion rate which increased slightly with time, following the injections, and which then decreased much more slowly than in the animals given radium by mouth. In the injected animals the rate of radium excretion decreased by one-half approximately every two weeks. This rate of decrease is much slower than was noted in Series II. The route of administration should not affect the rate of excretion of metabolic radium. The unabsorbed radium in the ingestion experiments would be eliminated within five days and subsequent excretions represent the elimination of metabolized radium. Direct gamma-ray at the site of injection and had only recently entered the body circulation.

During life these injected animals also exhibited only about 60 to 75 per cent of their radium as radon in their exhaled breath. Taking the average value of radon exhaled from the skeletal radium as 85 per cent, as found in Series I and II, this smaller fractional radon exhalation rate shows that the circulation of blood through the skeletal parts was much greater than through the area where the undiffused injected radium was entrapped in the dermal tissues. It is likely that a greater fraction of the radon produced in this area disintegrated without being carried by the blood stream to the lungs for exhalation.

In Series III, the fractional retention of radium actually reaching the circulation can be estimated by excluding the radium found in the tissues. Taking only the radium in the organs and skeleton and excreta, the fractional retention is $1.5/(1.5+1.5) = 50$ per cent for animal No. 20953, and $0.94/(0.94+0.9) = 51$ per cent for animal No. 20954. Thomas and Bruner[27] found about 25 per cent retention of radium chloride injected subcutaneously in rats.

bones of a rat (No. 16212) whose tibia was accidentally broken while roentgenograms were being taken seventy days after the beginning of the radium feeding period. At this time the radium was primarily located in the skeleton. Roentgenograms showed a dense structure at the area where the bone had healed. Autoradiographs (Fig. 14) show that there was also a high concentration of radium in this area.

The radium concentration in the osteo-

Table III

CALCIUM, PHOSPHORUS AND RADIUM CONTENT OF TIBIA AND FIBULA OF RADIUM POISONED RAT AND CONTROL RAT

| Tissue | Weight | Extracted Dry Weight | | | Ra/Ca |
|---|---|---|---|---|---|
| | | Calcium | Phosphorus | Radium | |
| | (gm.) | (gm./gm.) | (gm./gm.) | (gm./gm.) | (gm./gm.) |
| Tibia epiphysis | 0.15 (0.12) | 0.17 (0.15) | 0.08 (0.07) | $210\times10^{-9}$ | $1.3\times10^{-6}$ |
| Tibia shaft | 0.28 (0.22) | 0.22 (0.21) | 0.11 (0.10) | 400 | 1.8 |
| Femur epiphysis | 0.16 (0.10) | 0.18 (0.20) | 0.08 (0.09) | 250 | 1.4 |
| Femur shaft | 0.38 (0.15) | 0.21 (0.17) | 0.10 (0.08) | 350 | 1.7 |

In these analyses the right legs of rat No. 16835 were used. Bones were separated then cut through the metaphysis. Analyses on control No. 16216 are given in parenthesis.

Mention should be made of the fact that the administration of radium causes a hypercalcification of the long bones. This is evident in Figure 13 which shows an intense shadow in the metaphyseal areas of the tibia and femur, indicative of dense calcium deposits. Chemical analysis has shown that there is a tendency for these bones to contain more ash, calcium and phosphorus than the tibia and femur of a control animal (Table III). As these rats were young adults, these results indicate that a different type of bone was produced after the radium was administered.

A similar observation was made on the genic sarcoma of animal No. 16834 was $37\times10^{-9}$ grams Ra per gram of tumor, or only about 10 per cent of the radium concentration in the skeletal bones of the same animal, but the calcium concentration was not measured.

The distribution of radium in whole bone is not uniform (Fig. 14). These autoradiographs were made by sectioning the bone with a razor blade, mounting at the surface of a paraffin block and then placing on a photographic plate (Wratten and Wainright, Metallographic) with a thin sheet of cellophane separating the section from the photographic emulsion.

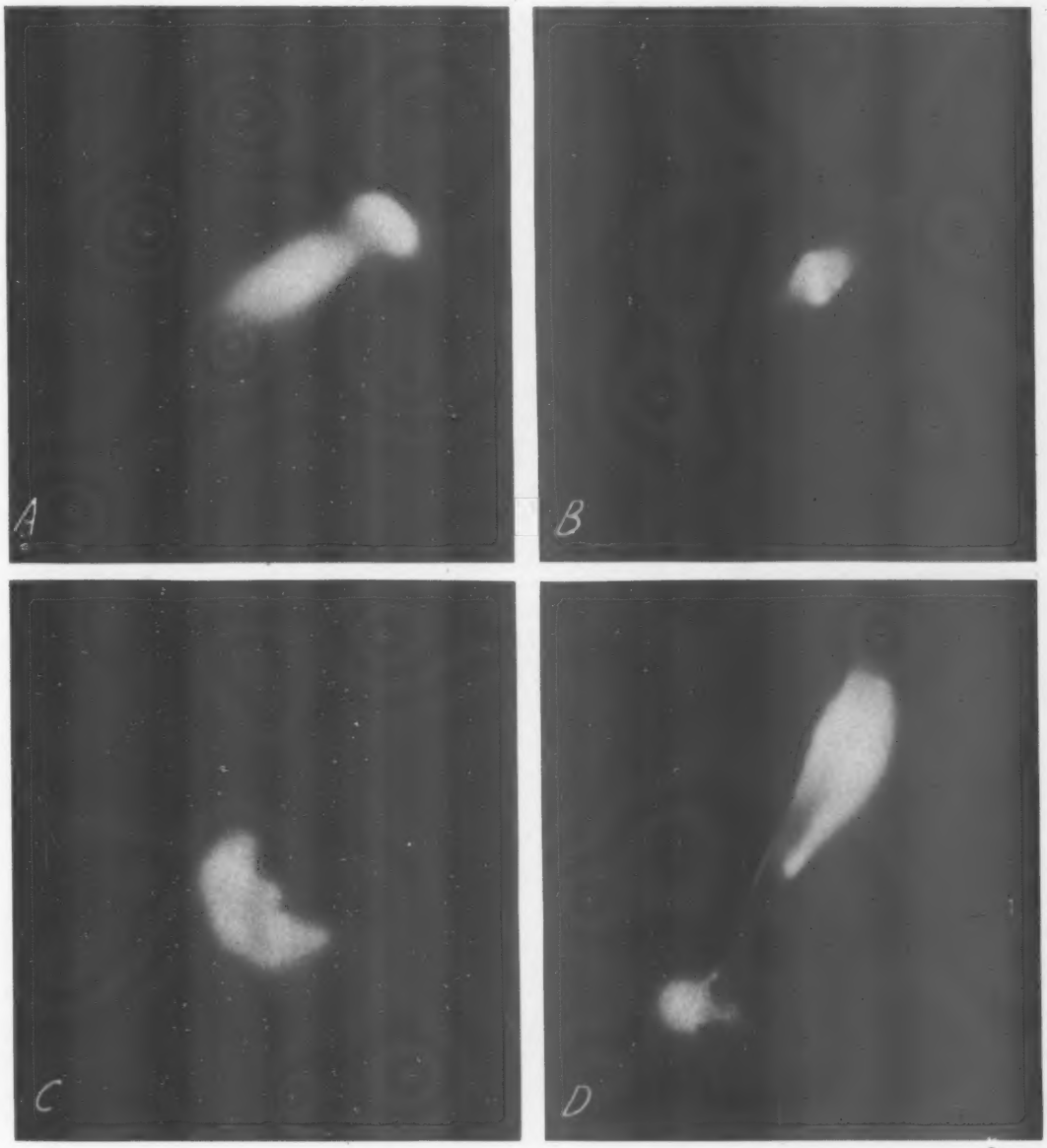


Fig. 14. Autoradiographs of bones. *A*, normal humerus of rat No. 16834. *B*, broken and healed humerus of rat No. 16834. *C*, broken and healed humerus of rat No. 16212, broken seventy days after radium feeding was begun, and noted fully healed five months later. *D*, normal vertebra of rat No. 16212.

While the living animals were being roentgenographed, the leg bones of several were broken. As this occurred with none of the control animals, it is evident that the bones of the radium treated rats were brittle. This is in agreement with the previous observation by Thomas and Bruner.[27]

### BLOOD FINDINGS

On November 23, 1937, 386 days after the animals in Series 1 had been given radium orally, a sample of blood was taken from the test and control rats and analyzed. The results are shown in Table IV.

With the exception of No. 16213, all

TABLE IV

RESULTS OF ANALYSES OF BLOOD TAKEN FROM SERIES I AND II CONTROLS, 386 DAYS AFTER RADIUM WAS FED

| Rat number | 16215 | 16216 | 16212 | 16213 | 16214 | 16834 | 16835 |
|---|---|---|---|---|---|---|---|
| Probable Ra Dosage (micrograms) | 0 | 0 | 22 | 28 | 10 | 62 | 70 |
| Red cells (million/mm.$^3$) | 7.8 | 7.6 | 2.2 | 7.0 | 6.8 | 7.3 | 2.9 |
| White cells (thousands/mm.$^3$) | 12.8 | 11.2 | 10.4 | 19.0 | 14.6 | 5.4 | 12.0 |
| Small lymphocytes (per cent) | 29.0 | 29.0 | 21.0 | 32.0 | 26.0 | 20.0 | 37.0 |
| Large lymphocytes (per cent) | 16.0 | 21.0 | 20.0 | 8.0 | 12.0 | 31.0 | 16.0 |
| Monocytes (per cent) | 15.0 | 21.0 | 4.0 | 6.0 | 10.0 | 11.0 | 13.0 |
| Eosinophils (per cent) | 0.0 | 1.0 | 4.0 | 0.0 | 1.0 | 2.0 | 0.0 |
| Hemoglobin (gm/100 cc.) | 9.8 | 9.4 | 8.7 | 8.2 | 9.2 | 8.4 | 4.5 |

TABLE V

RELATIVE MAINTENANCE AND TOXIC DOSES OF VITAMINS AND MINERALS PER KILOGRAM WEIGHT[1] OF MAN AND RAT

| Substance | Grade of Toxicity | Per Kilogram | | Rat/Man Ratio |
|---|---|---|---|---|
| | | Rat | Man | |
| | | Maintenance Dose[2] | | |
| Vitamin A | | 180 IU | 70 IU | 2.6 |
| Vitamin D | | 18 IU | 6 IU | 3.0 |
| Thiamine | | 0.060 mg. | 0.026 mg. | 2.3 |
| Riboflavin | | 0.075 mg. | 0.039 mg. | 1.9 |
| Iron | | 0.75 mg. | 0.17 mg. | 4.4 |
| Calcium | | 154 mg. | 11 mg. | 14.0 |
| Phosphorus | | 180 mg. | 14 mg. | 12.9 |
| | | Toxic Dose[3] | | |
| Arsenic[4] | Chronic | 0.05 mg. | 0.01 mg. | 5.0 |
| Barium[5] | Acute | 118 mg. | 11 mg. | 10.7 |
| Copper[6] | Acute | 35 mg. | 7 mg. | 5.0 |
| Lead[7] | Acute | 3556 mg. | 142 mg. | 25.0 |
| Lead[8] | Chronic | 2.13 mg. | 0.014 mg. | 152.0 |
| Mercury[9] | Acute | 36.6 mg. | 14 mg. | 2.5 |
| Radium[10] | Chronic | 0.003 mg. | 0.00002 mg. | 150.0 |
| Selenium[11] | Chronic | 0.3 mg. | 0.05 mg. | 6.0 |
| Thallium[12] | Acute | 25.0 mg. | 10.0 mg. | 2.5 |

[1] Calculations are based on 70 kg. man and 0.33 kg. rat.

[2] The vitamin and mineral allowances for man are those of the National Research Council.[a] Maintenance dose for rats represents usual allowances in nutrition research.

[3] With the exception of radium data, the toxic doses and appended notes were prepared by Dr. H. O. Calvery of the U. S. Food and Drug Administration.

[4] Arsenic figures for man derived from report of the Royal Commission appointed to inquire into the Manchester beer poisoning.[b]

[5] Barium dose for man is the probable fatal dose (Sollmann[c]): that for rat is $LD_{50}$ as determined in the laboratories of the Division of Pharmacology of the U. S. Food and Drug Administration.

[6] Copper dose for man is emetic dose (Sollmann[c]): dose for rat is that causing depressant effect as determined by the Division of Pharmacolcgy of the U. S. Food and Drug Administration.

[7] Acute dose of lead for man is lowest reported fatal dose (Sollmann[c]): doses for rats are $LD_{50}$ for lead acetate as determined by the Division of Pharmacology of the U. S. Food and Drug Administration.

[8] Chronic dose for man is taken from data of Kehoe and coworkers[d] where the blood and urine lead, in the case of two individuals, receiving known amounts of lead three times daily, in a well-controlled experiment over a long period of time, reached levels often

radium-fed rats showed polychromatophilia. Rats No. 16212 and 16835 showed anisocytosis. Rats No. 16834 and 16835 both showed increased nucleated red cells, indicating abnormal functioning of the bone marrow.

There was no correlation between the red cell count and the amount of radium in the bodies of the rats, though the red cell count of all test animals was lower than that of the controls. Two showed very low red cell counts and in 1 of these (No. 16835) the hemoglobin reading was also low.

The white cell data were variable and do not bear a relationship to the radium content. The high value in No. 16213 may be the result of an infected leg which he had at the time. Rat No. 16835 had the poorest blood picture and was the only one who had exhibited tumors when these samples were taken.

### EFFECT OF RADIUM ON DISTRIBUTION OF BONE CALCIUM

The roentgenograms of radium poisoned rats all show an opacity in the metaphyseal region, indicating hypercalcification (Fig. 13). An attempt to confirm this by chemical analysis was made by study of the right femur and tibia of rats No. 16835 (radium fed) and No. 16216 (control). The bones were prepared by severing the flesh-free bones axially near the metaphysis with a razor blade. The resulting specimens were weighed, dried, extracted, weighed, ashed, weighed and then analyzed for calcium and phosphorus content. The results of these analyses are presented in Table III. There does not seem to be a significant difference between the two series of results.

Of especial interest is the average ratio of radium to calcium ($1.5 \times 10^{-6}$) presented in Table III. Examination of the tibia and fibula of one human subject[1] who died with osteogenic sarcoma resulted in a Ra/Ca ratio of $6 \times 10^{-9}$, or 250 times lower.

One may conclude from this that the rat is not an acceptable animal for the estimation of the lethal dose of radium in man. Extrapolation of rat results on the basis of body weight, body surface, skeletal weight or blood volume does not approximate the lethal dose for man. A similar conclusion was reached recently by Calvery.[3] That body weight is a doubtful basis for extrapolating data obtained on man or rat is shown clearly in Table V which presents the estimates of therapeutic and toxic

observed in cases of recognized lead poisoning, although these two individuals were not reported to show other signs of lead poisoning. Chronic dose for rat is the smallest to produce symptoms with lead acetate.[e,f]

[9] Mercury dose is for bichloride. Human dose is that reported by Sollmann[c] as having survived prompt treatment, but fatal otherwise. Rat dose is $LD_{50}$ as determined by the Division of Pharmacology of the U. S. Food and Drug Administration.

[10] Radium dose for humans is taken from recent unpublished measurements by H. S. Martland, J. C. Aub, and R. D. Evans on three patients containing 0.9, 1.1, and 1.5 micrograms of radium. Death from radium poisoning has been observed in one patient containing only 0.5 microgram of radium.[g] Rat data taken from animals No. 16212 and 16213 who died with osteogenic sarcoma. The radium doses, for both man and rat, refer to radium *retained* in the body.

[11] Selenium dose for man is the median estimated dose to produce symptoms as calculated by M. I. Smith and coworkers.[h] Dose for rat is lowest dose producing definite pathological changes as found by the Division of Pharmacology of the U. S. Food and Drug Administration.

[12] Thallium dose for man is that reported as toxic but allowing recovery.[i] Dose for rat is that given by Sollmann and Hanzlik[i] as the minimum lethal dose.

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doses of a selected group of compounds and elements. The rat/man ratio, on the basis of equal body weights, varies between 2 and 152.

SUMMARY

1. Chronic radium poisoning has been studied in four series of young adult male Wistar rats; twenty-one were given radium by mouth, and three by intradermal injection.

2. Apparatus is described for measuring the radium content of living rats, using gamma rays from the body and the radon content of the exhaled breath. The breath radon accounts for 85 per cent of the radium content of the living animal. Radium measurements were also made on the excreta, and on postmortem material.

3. Oral administration of 25 to 100 micrograms of radium resulted about a year later in a high incidence of primary osteogenic sarcoma, usually in the vertebrae and with metastases in the lung and other organs. The sarcomas are transplantable. Pathological findings are reported.

4. Following oral administration over a period of ten to twenty days, only 4 to 8 per cent of the radium was retained in the animal four days after the last feeding.

5. At death, 1 to 7 per cent (average 3 per cent) of the radium administered orally remained in the animal's body. About 50 per cent of the radium injected intradermally was retained at death. A terminal retention of 1 microgram of radium is sufficient to produce osteogenic sarcoma. At death, over 90 per cent of the retained radium is found in the skeleton. The bones show at least 100 times the radium concentration of the richest soft tissue (lung).

6. Many of the classical symptoms of chronic radium poisoning in human beings were exhibited by these animals. The radium stimulates a hypercalcification at the ends of the long bones. The bones become fragile, but heal satisfactorily, exhibiting a marked concentration of radium at the site of repair.

7. The incidence of anemia was low. Only moderate disturbances of the normal blood picture were noted, and there was no correlation with the radium content of the various animals.

8. The rat cannot be used for obtaining an estimate of the toxic dose of radium in man. It is shown that the toxic dose, per kilogram body weight, is greater in the rat than in man by factors varying from about 2.5 to 150 for eight toxic metals. To produce chronic symptoms similar to those in man, the rat requires some 150 times as much radium per kilogram body weight, and some 250 times the skeletal ratio of radium to calcium as does man.

We wish to record our thanks to Dr. Herbert O. Calvery and Dr. J. C. Aub for many stimulating discussions during the course of these experiments, to Dr. Shields Warren, Dr. Clifford Franseen, Dr. Olive Gates, and Miss R. McLean for the pathological studies, and to Dr. Austin Brues for preparing the photomicrographs of the pathological sections.

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# INTRATHORACIC HODGKIN'S DISEASE*

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THE typical case of Hodgkin's disease with discrete, painless enlargement of peripheral lymph nodes is well known and has been thoroughly described. However, not only peripheral lymphoid tissue but also that of the spleen, bone marrow, lungs, pleura, liver, muscles, skin and digestive tract may be involved; and the frequency of such involvement is less well recognized. The intrathoracic manifestations of Hodgkin's disease are of particular interest because of the varied character of the disease in the chest, and its close similarity to other more common lesions of the lungs.

A series of histologically proved cases of Hodgkin's disease has been studied from the standpoint of intrathoracic involvement including that of mediastinal lymph nodes, pulmonary parenchyma, pleura, heart and bony thorax. This study was prompted by the observation of several cases referred with a diagnosis of pulmonary tuberculosis which on further observation were found to be intrathoracic Hodgkin's disease without evidence of tuberculosis. This series has been reviewed to determine what proportion shows intrathoracic involvement which might, therefore, be confused with some other disease of the chest. In all cases the diagnosis was proved by autopsy or biopsy or both. Not included in this series are cases of other lymphomatoid diseases such as lymphosarcoma. While the latter may have similar roentgenologic findings and follow much the same clinical course, this study is of Hodgkin's disease alone.

## INCIDENCE

It is recognized that the only unequivocal way to demonstrate intrathoracic disease is by chest roentgenography, biopsy, or autopsy. The limitations of physical examination alone are apparent, for only masses of relatively large size are recognized by their physical signs or by symptoms produced by their location. Furthermore, these physical signs of tumor are not pathognomonic of Hodgkin's disease alone. Only proved cases, therefore, have been collected in this series studied by autopsy or biopsy, and in which roentgenograms were available. There are 55 such cases. Of these, 35 cases, or 63 per cent, showed intrathoracic involvement.

## CLASSIFICATION

Numerous classifications of intrathoracic Hodgkin's disease have been proposed.[5,9,13,15] For the purposes of study and presentation, these cases have been grouped according to the involvement of the main anatomical structures of the thorax, that is, the mediastinum, thymus gland, lung, pleura, heart and bony cage. It must be recognized that because of the tendency of this disease to be widely disseminated most cases will overlap from one type to another, and the classification is determined by the structure which is predominantly involved. Fifteen cases have been selected to illustrate the varied involvement of the organs of the thorax under the headings of (I) *mediastinal*, (II) *parenchymal*, (III) *pleural*, (IV) *osseous* and (V) *cardiac types*.

Regardless of the etiologic factors concerned, Hodgkin's disease is characterized anatomically by marked involvement of lymphoid tissue. The character of the disease in any organ, or region of the body, will therefore be determined by the location of its lymphoid tissue and the degree to which it is affected by the etiologic factor. The protean manifestations of intrathoracic Hodgkin's disease can be correlated with the anatomical distribution of lymphoid tissue within the chest, for it is abun-

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dantly supplied with such tissue of which the three major accumulations are those of the mediastinum, lung parenchyma and pleura.

I. *Mediastinal Types*

The mediastinal variety is the most common in this series since 50 per cent of the cases fall in this group. The mediastinum contains an extensive collection of lymph nodes consisting of the small nodes of its anterior and posterior divisions; the more numerous nodes extending along the trachea (the paratracheal nodes); the nodes in the hilum at the angles of the trachea and major bronchi, and in the carina (the tracheobronchial nodes); and those at the angles of the larger bronchial branches (the bronchopulmonary nodes).

The manifestations of the disease will depend on the extent and degree to which these various groups of nodes are affected. If the nodes are generally involved, massive, lobulated mediastinal shadows are noted in the roentgenogram (Case III). More frequently, however, discrete enlargement of nodes is present. In our series, the hilar nodes are the most commonly involved, the localized enlargement suggesting other lesions such as carcinoma, tuberculosis and sarcoid (Case I). Enlargement of the right paratracheal nodes has been emphasized by several authors,[9,13,14] although it was not a prominent feature in our series.

Clinically, these patients present the usual signs and symptoms associated with Hodgkin's disease. Irritative cough and shortness of breath are common, particularly in those individuals with generalized, massive involvement of the mediastinal lymph nodes. The roentgenologic manifestations are likewise not pathognomonic, for they may appear in many other lesions of the chest. The diagnosis depends on biopsy of peripheral nodes or other accessible material.

Case I. J. I., white male, aged thirteen, complained of swelling of the neck, weight loss and headache. Large bilateral cervical nodes and a palpable spleen were found on examination. The temperature curve ranged from 38° to 40° C. Biopsy of a cervical node established the diagnosis of Hodgkin's disease. For several months there was fair response to high voltage roentgen therapy, but the patient died four years after the onset of the disease. At autopsy (Dr. Paul Gross) the diagnosis was confirmed by finding enlarged, discrete and firm lymph nodes in the mediastinum in the region of the main stem bronchi. The spleen was enormously enlarged (575 gm.) and diffusely infiltrated with nodular masses. Roentgenogram of the chest (Fig. 1) showed marked localized involvement of the right hilar nodes.

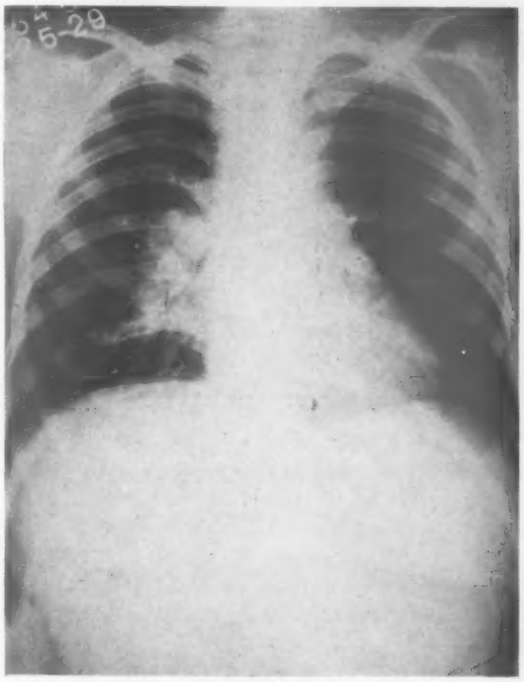

Fig. 1. Case I. Mediastinal type. Large group of right hilar nodes.

Case II. J. S., white male, aged forty-seven, complained of hoarseness, cough, chest pain radiating to the right shoulder, fever and swelling of the neck. There was widening of the retrosternal dullness. Basal metabolic rate was plus 15. A tentative diagnosis of a substernal thyroid gland was made. However, a supraclavicular node measuring 5 mm. in diameter which was removed for biopsy proved to be early Hodgkin's disease. Radiation therapy caused retrogression of the involved nodes in the para-

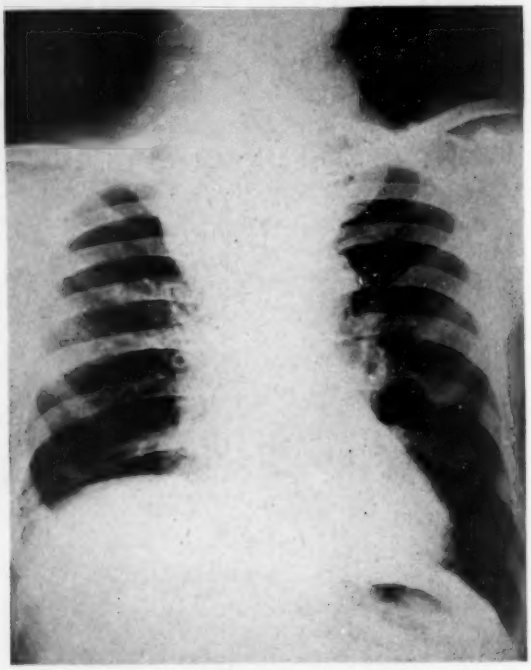

Fig. 2. Case II. Mediastinal type. Paratracheal nodes enlarged bilaterally.

tracheal regions. The patient was progressing satisfactorily four years after the onset of the disease. Roentgenogram of the chest (Fig. 2) showed bilateral enlargement of the paratracheal nodes.

Case III. J. B., white female, aged fifty-one, had swelling of the right side of the neck. Examination showed enlarged right supraclavicular lymph nodes with an increase in the retrosternal dullness. Biopsy of a node revealed Hodgkin's disease. There was marked retrogression following roentgen therapy. Fifteen months later the patient had a relapse with fever and enlargement of the liver and spleen. Three doses of 200 r were administered over the liver and spleen, but no further therapy was given due to the presence of a neutropenia. The patient died sixteen months after the onset of the disease from pyemia and agranulocytosis. Autopsy (Dr. A. E. Margulis) revealed hyalinization and fibrosis of the irradiated paratracheal nodes, and Hodgkin's disease of a celiac lymph node. Roentgenogram of the chest (Fig. 3) showed diffuse enlargement of the paratracheal and hilar nodes producing a massive mediastinal shadow.

II. *Parenchymal Types*

Involvement of the lung parenchyma occurred in 40 per cent of the series and represents the second most common type. These patients are likely to present the most confusing diagnostic problems because of the wide variety of roentgenologic manifestations which can be produced. It is this type which so closely simulates tuberculosis, pneumonia, bronchogenic carcinoma, sarcoidosis, pulmonary abscess and pulmonary metastases. It must be emphasized that frequently no clear-cut distinction can be drawn between the various types of intrathoracic involvement which are described. Combinations occur commonly, particularly the association of pulmonary and pleural lesions with enlargement of the mediastinal nodes.

*Infiltrative lesions.* The lung may be involved in Hodgkin's disease in numerous ways. Frequently the pulmonary lesions are produced by direct infiltration of the lung from mediastinal nodes. This invasion oc-

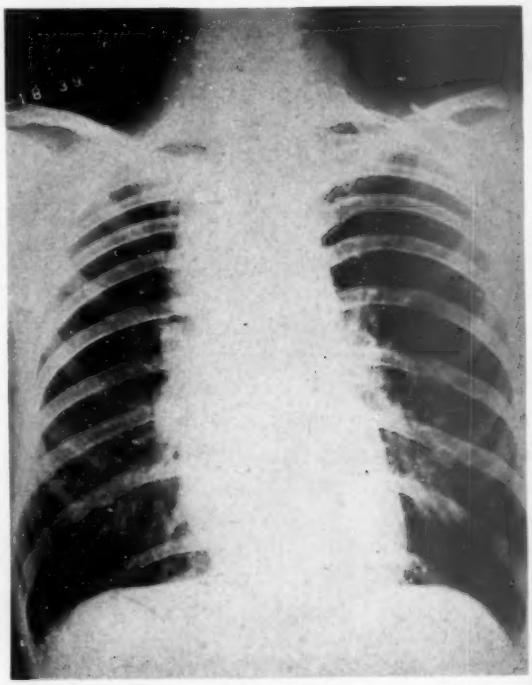

Fig. 3. Case III. Mediastinal type. Right paratracheal and hilar nodes, moderately enlarged.

curs as a solid growth which extends across the mediastinal pleura into the parenchyma to produce the picture of a massive tumor of the lung (Case v). These cases may be readily confused with bronchogenic carcinoma.

The lung itself contains an abundance of lymphoid aggregates. It has been shown[10] that follicles and small collections of lymphoid cells are present at points of bronchial branching, situated between the tunica muscularis and the accompanying artery. Similar collections are found at points of division of the pulmonary arteries, lying between the vessel wall and the adjacent alveoli. Lymphoid tissue is also found at points of junction of the pulmonary veins.

A frequent mode of extension is by infiltration of the disease along the peribronchial and perivascular lymphatics and lymphoid tissue, resulting in a granulomatous bronchitis and peribronchitis.[11] The bronchi appear encased in granulomatous tissue and may even be occluded. Roentgenologically, this type of extension reveals itself as linear or feathery infiltrations extending into the lung field from the hilum (Cases iv and vi).

Another infiltrative lesion occurs by extension of the disease through the alveoli, producing a granulomatous consolidation of the lung. This may be of lobar distribution resembling the appearance of a pneumonia (Case viii). However, it may be lobular in character, and, situated in the upper lobes, these small areas of involvement may closely resemble pulmonary tuberculosis (Case vii).

Case iv. B. U., white female, aged twenty-seven, first entered the hospital in December, 1929, because of cervical node enlargement of one month's duration. Biopsy revealed the presence of Hodgkin's disease. Roentgen therapy caused clinical remission of the disease. In January, 1938, she developed cough and shortness of breath. Physical signs of infiltration of the left upper lobe developed. Further irradiation produced satisfactory remission. She then developed symptoms of cardiac failure which responded to roentgen therapy. However, later involvement of abdominal nodes occurred with progression of the disease and ultimate death in June, 1940, ten years and seven months after the onset of the disease. Autopsy (Dr. A. E. Margulis) showed involvement of the right lung, mediastinum, heart and spleen by Hodgkin's disease. Roentgenogram of the chest showed mediastinal enlargement with extension into the left lung (Fig. 4*A*), bilateral diffuse involvement (Fig. 4*B*), and retrogression of the lesions following roentgen therapy (Fig. 4*C*).

Case v. A. H., white male, aged twenty-four, was admitted to the hospital because of cough, chills, chest pain, fever, diarrhea and pruritus. The cervical nodes were enlarged and the fever persisted. Biopsy of a cervical node revealed Hodgkin's disease. There was poor response to irradiation and the patient died eight months after admission. Roentgenogram of the chest (Fig. 5) showed massive mediastinal involvement with invasion of the right lung. The disease had extended from the nodes of the right hilum and paratracheal region into the parenchyma of the lung.

Case vi. S. B., white male, aged thirty-five, was referred because of enlargement of the left supraclavicular lymph nodes. The diagnosis of Hodgkin's disease was made by biopsy. Parenchymal involvement developed which responded favorably to irradiation. There was clinical remission of the disease for several months, but the patient then followed a retrogressive course and death occurred two years after the onset of the disease. Roentgenograms of the chest (Fig. 6*A*) showed a linear infiltration radiating from the left hilum which retrogressed considerably after treatment (Fig. 6*B*).

Case vii. A. R., white female, aged thirty, was admitted to the tuberculosis pavilion of the hospital because of cough and fever. Four years previously at another institution an enlarged cervical node had been removed and a diagnosis of Hodgkin's disease established. Roentgen therapy had also been administered at that time. During the present admission thorough examination showed no evidence of tuberculosis. Biopsy of another cervical node revealed Hodgkin's disease with irradiation changes. The patient responded poorly to irradiation and died seven months after admission. Autopsy (Dr.

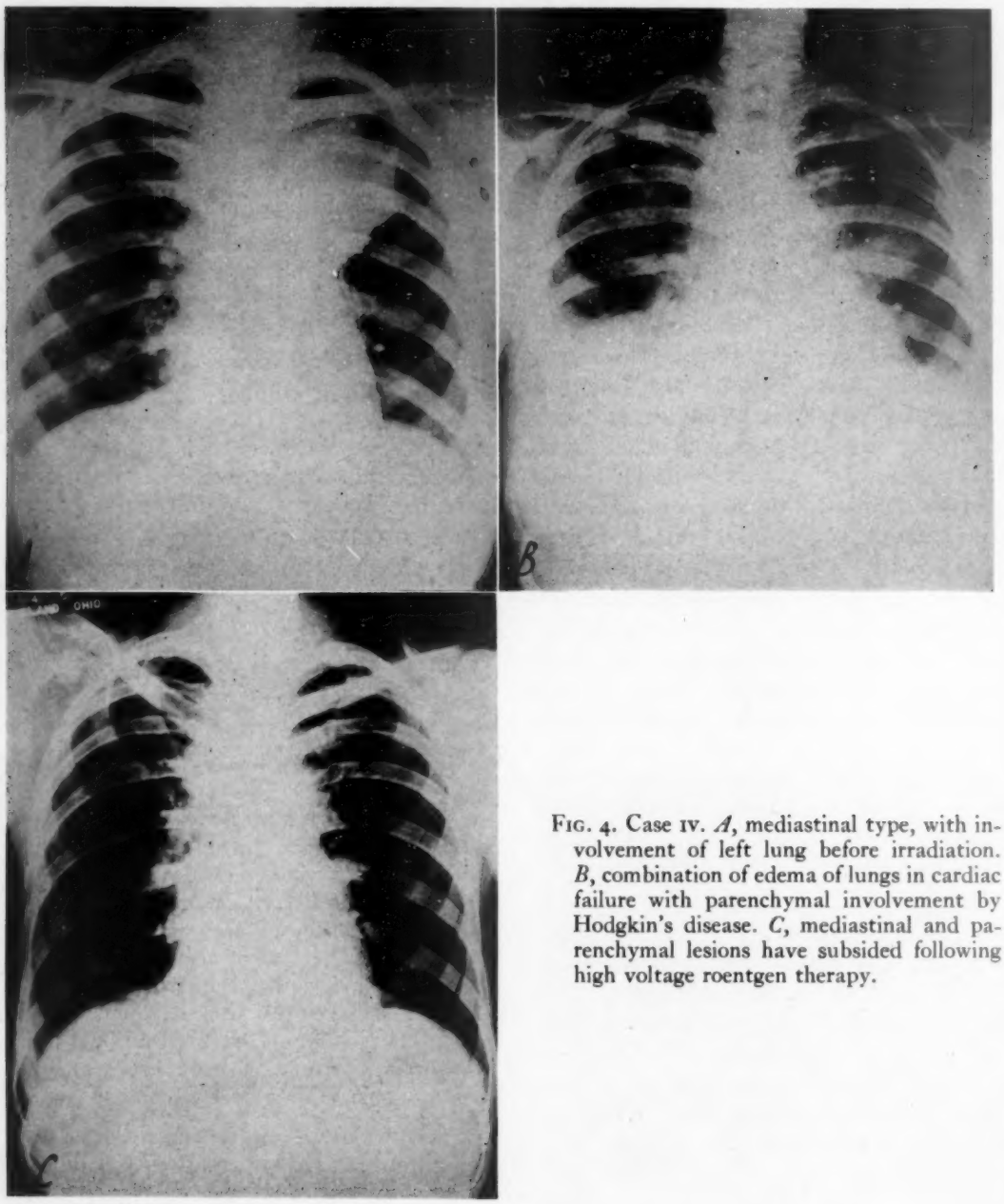

FIG. 4. Case IV. *A*, mediastinal type, with involvement of left lung before irradiation. *B*, combination of edema of lungs in cardiac failure with parenchymal involvement by Hodgkin's disease. *C*, mediastinal and parenchymal lesions have subsided following high voltage roentgen therapy.

R. P. Moore) revealed a spherical mass of Hodgkin's tissue 9 cm. in diameter extending from the right hilum to the upper, middle and lower lobes. Extensive fibrosis in the lesion was thought to represent irradiation changes. Roentgenograms of the chest (Fig. 7, *A* and *B*) showed diffuse parenchymal infiltration in the right middle and upper lung fields. The appearance of the latter could readily be confused with tuberculosis.

CASE VIII. E. B., white male, aged twenty-eight, was admitted to the hospital because of weight loss, pain in the left shoulder, fever and enlargement of the cervical lymph nodes. Biopsy showed Hodgkin's disease to be present. Roentgenograms of the chest (Fig. 8, *A* and *B*) showed dense mottling in the right lung field. The lateral view demonstrates a homogeneous density of the right middle lobe simulating pneumonic consolidation. Autopsy (Dr. C. M.

Blumenfeld) showed involvement of numerous organs including lung, pleura, diaphragm and mediastinal nodes. The right middle lobe was reduced in size, firm and infiltrated with pale gray to pale yellow masses.

*Nodular lesions.* A less frequent manifestation is the occurrence of well circumscribed, isolated nodules which closely simulate the roentgen appearance of pulmonary metastases. In our cases these isolated nodules were usually accompanied by other manifestations of Hodgkin's disease within the thorax, particularly involvement of the mediastinal nodes. It cannot be stated with certainty whether these circumscribed nodules arise as independent foci of Hodgkin's disease in pulmonary lymphoid aggregates or whether they are produced by extension of the disease along peribronchial and perivascular lymphatic channels.

In this series there have been no examples of the miliary lesions of the lungs such as that described by Vieta and Craver.[12]

Fig. 5. Case v. Massive mediastinal involvement with invasion of the lung. The disease has extended from the right hilum and paratracheal nodes to the right upper lobe.

Case ix. E. S., white female, aged forty-five, was admitted to the tuberculosis service because of cough, expectoration, loss of weight and fever of ten months' duration. Later there

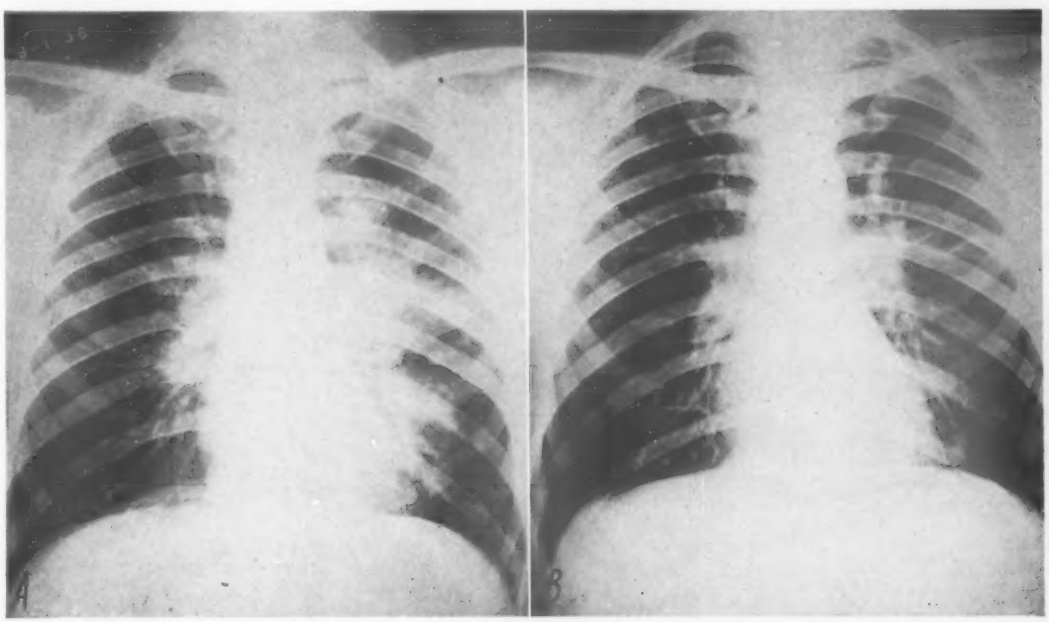

Fig. 6. Case vi. *A*, diffuse parenchymal infiltration radiating from the left hilum before irradiation. *B*, diffuse parenchymal involvement almost completely disappeared following treatment by high voltage roentgen rays.

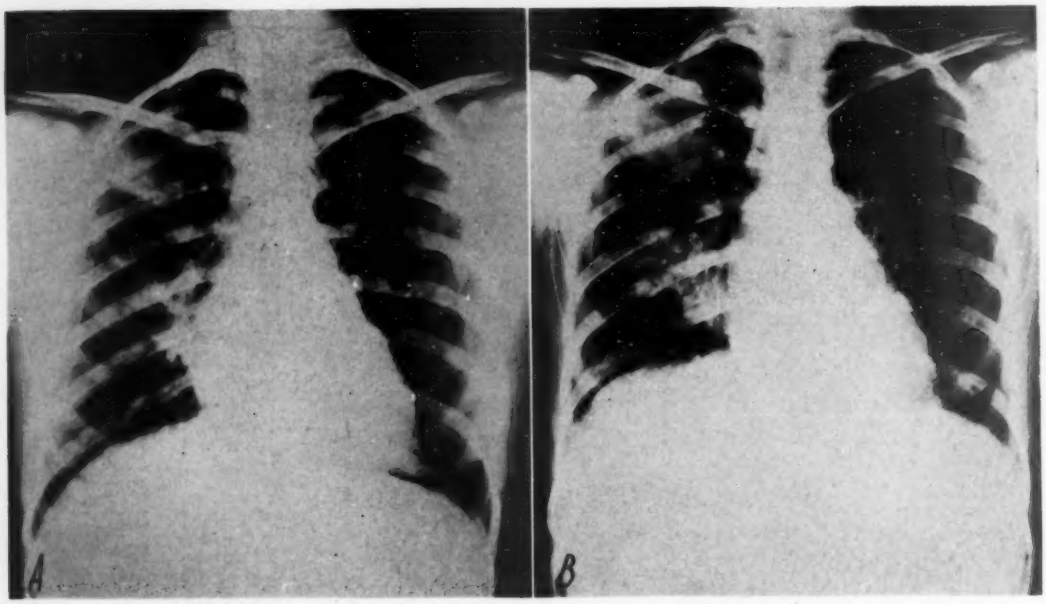

FIG. 7. Case VII. *A*, diffuse parenchymal infiltration in the right upper lobe. *B*, diffuse parenchymal infiltration, more extensive in the right lung. Unaffected by radiation therapy.

developed a serous effusion on the right which necessitated several thoracenteses. The sputum was constantly negative for tubercle bacilli. The patient died three months after admission to the hospital. Autopsy (Dr. M. R. Oldt) revealed extensive Hodgkin's disease of the lungs,

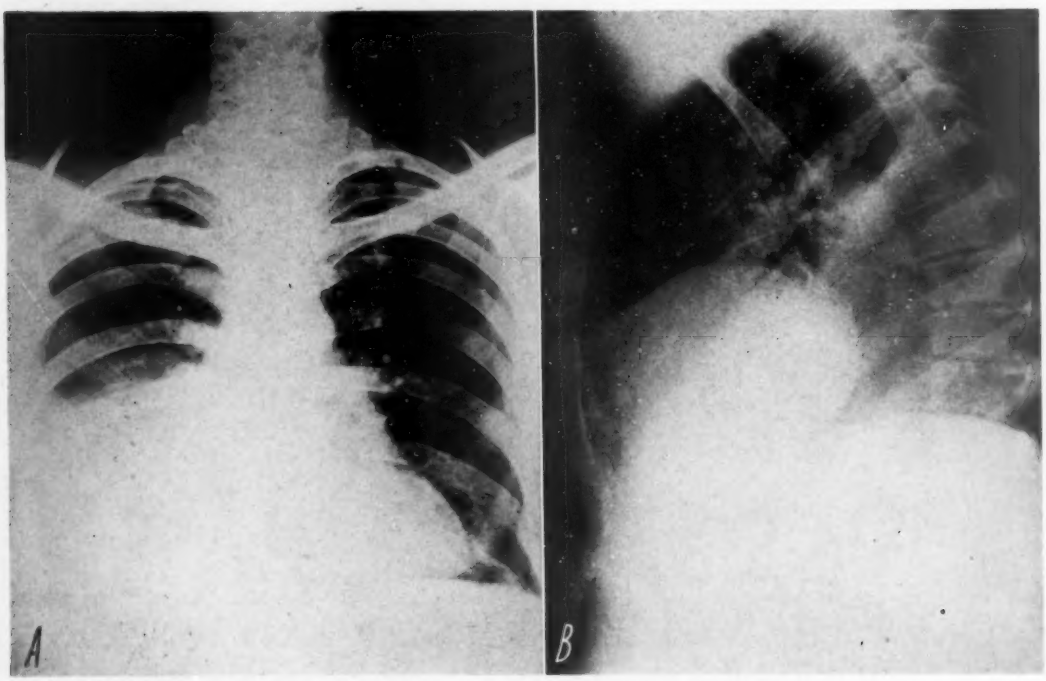

FIG. 8. Case VIII. *A*, lobar distribution of Hodgkin's infiltration in right lower lung field. *B*, lateral view reveals infiltration to be located in the right middle lobe.

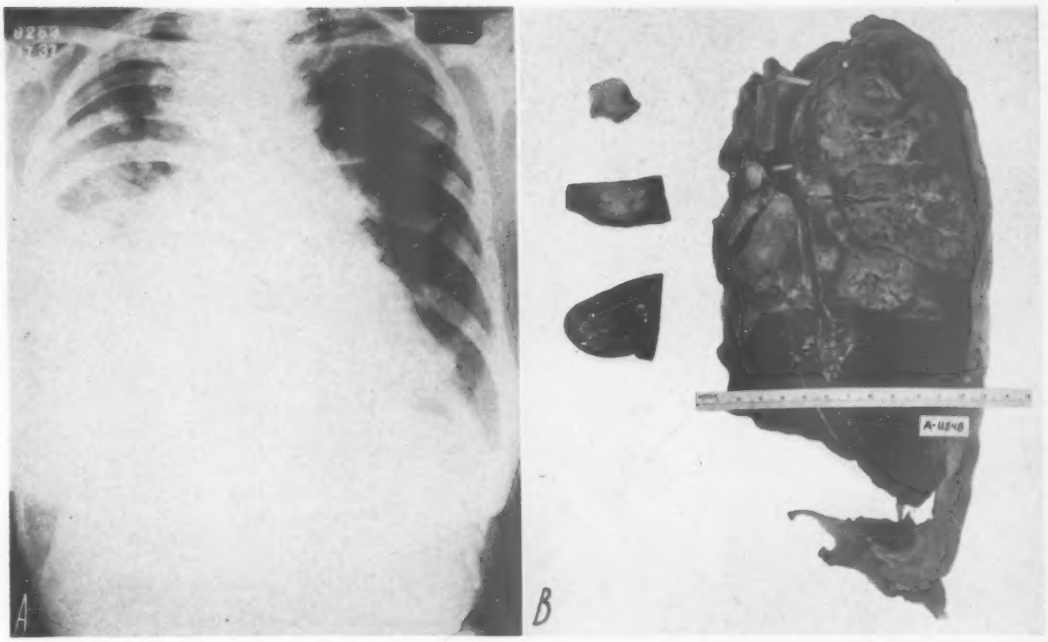

Fig. 9. Case IX. *A*, nodular infiltration in right upper, left upper and left lower lobes. Pleural effusion present on right. *B*, specimen of right lung. Nodular and diffuse infiltration viewed from posterior aspect.

pleura, liver, spleen and mediastinal lymph nodes. Roentgen examination of the chest (Fig. 9*A*) showed nodular infiltration of both upper lobes and the left lower lobe. There was a pleural effusion on the right. The pathologic specimen (Fig. 9*B*) shows the character of the infiltration in the right lung.

Case X. J. S., white female, aged twenty-eight, was admitted with the complaint of cough and fever. Biopsy of a cervical node revealed the presence of Hodgkin's disease. There was satisfactory remission of the disease until the patient became pregnant. She had a spontaneous delivery of a dead fetus at seven months. Following this mishap, there was poor response to treatment. Death occurred four years after the onset of the disease. Roentgenogram of the chest (Fig. 10) shows a large circumscribed nodular infiltration of the lower right lung field. The infiltration in the left lower lobe was somewhat more diffuse.

Certain other interesting parenchymal changes have been noted, such as atelectasis and cavitation.

*Atelectasis.* In addition to extension of Hodgkin's disease peribronchially, granulomatous ulcerations and plaques may occur within the bronchial wall,[11] or there may be actual invasion of the bronchus

Fig. 10. Case X. Nodular infiltration of large size in right lower lung. The lesion was unaffected by irradiation.

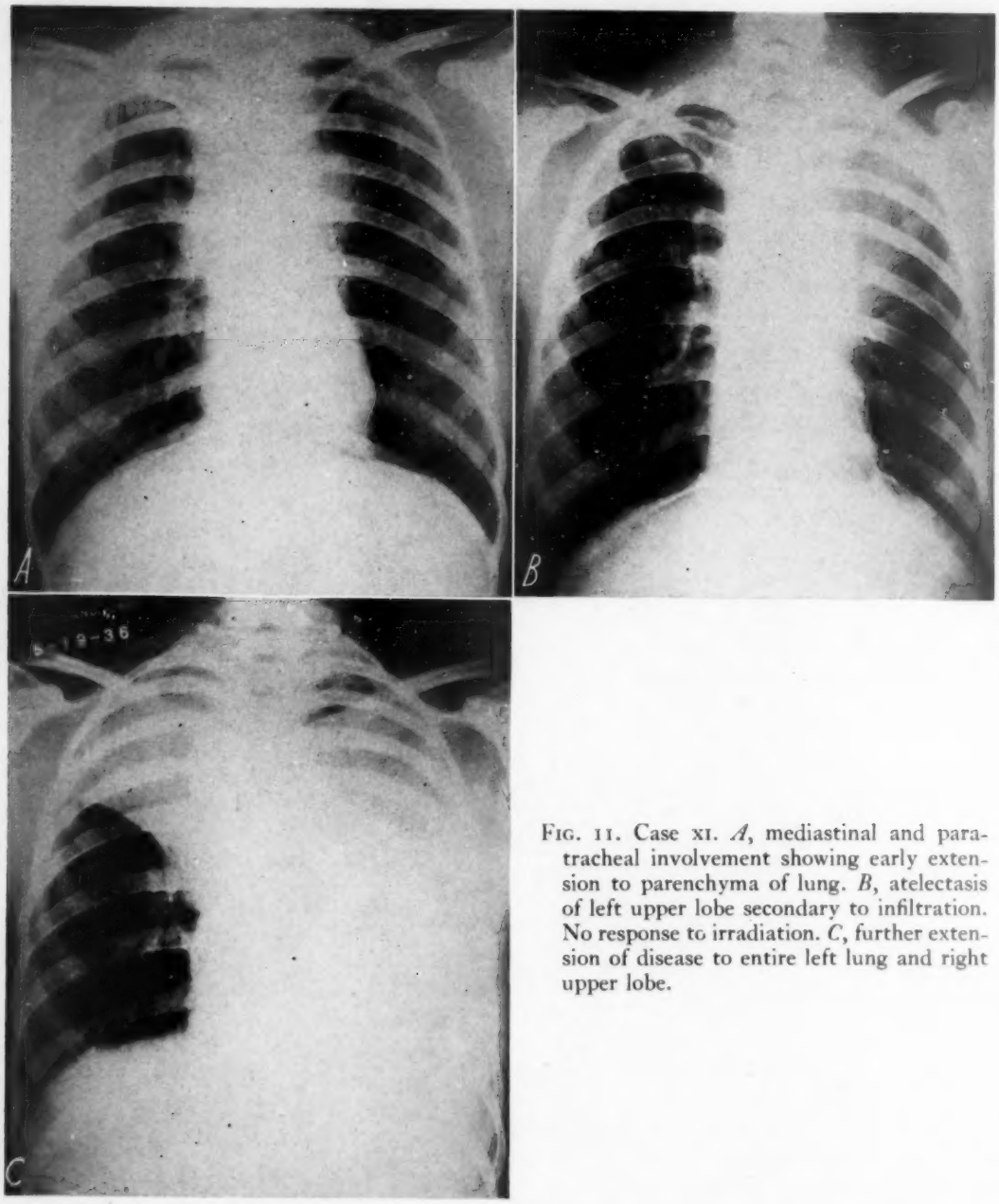


Fig. 11. Case xi. *A*, mediastinal and paratracheal involvement showing early extension to parenchyma of lung. *B*, atelectasis of left upper lobe secondary to infiltration. No response to irradiation. *C*, further extension of disease to entire left lung and right upper lobe.

from adjacent diseased lymph nodes. In such instances bronchial obstruction and atelectasis may occasionally be produced, simulating the appearance of bronchogenic carcinoma.[4,11] This change is usually a gradual process so that the extent of the collapse may be progressive (Fig. 11, *A*, *B* and *C*). In a few instances, bronchoscopic biopsy has established the diagnosis of Hodgkin's disease.[7,12]

Case xi. J. O., female, aged twenty-four, nurse, was admitted to the hospital because of loss of weight, fever and malaise. Biopsy of a small cervical lymph node revealed only a chronic granulomatous infiltration. However, a presumptive diagnosis of lymphoma was made

and the patient was given roentgen therapy. There was no improvement and she died one year after the onset of the disease. Roentgenograms of the chest (Fig. 11*A*) showed mediastinal and paratracheal involvement on the left. Later there was atelectasis of the left upper lobe (Fig. 11*B*) followed by extension to the entire left lung and consolidation of the right upper lobe (Fig. 11*C*). Autopsy (Dr. H. H. Heitzman) revealed extensive Hodgkin's involvement of the lungs, pleura and mediastinal nodes. There was granulomatous tissue in the left main-stem bronchus and in the right hilum which resulted in bronchial obstruction and atelectasis of the left lung and right upper lobe.

*Cavitation.* Cavitation occurs as a result of necrosis of Hodgkin's tissue within the lung and its extrusion through the tracheobronchial tree. In these instances microscopic examination shows the cavity wall to be lined by granulomatous tissue. This is an uncommon manifestation of intrathoracic Hodgkin's disease which may be confused particularly with tuberculosis, abscess and cavitary bronchogenic carcinoma. Examples have been described by Hardin,[4] Bouslog and Wasson,[1] and Vieta and Craver.[12]

Case xii. S. W., white female, aged sixty, entered the hospital because of weight loss of two years' duration. She had previously been considered to have either tuberculosis or carcinoma of the lung. Roentgenogram of the chest (Fig. 12) showed parenchymal infiltration of the right upper lobe with multilocular cavitation. Autopsy (Dr. F. M. Ruegsegger) revealed Hodgkin's disease of the right lung and mediastinal lymph nodes. The lesion of the right upper lobe was cavitated and the cavity wall microscopically contained granulomatous tissue.

Clinically, patients with parenchymal involvement present all the signs and symptoms usually associated with the more common pulmonary diseases. Cough, chest pain, fever, weight loss and night sweats are common. In the cavitary forms, purulent expectoration may occur. Hemoptysis is an interesting but uncommon complication. Usually it results from erosion of the bronchial mucosa but may likewise occur in the cavitary forms. The presence of such

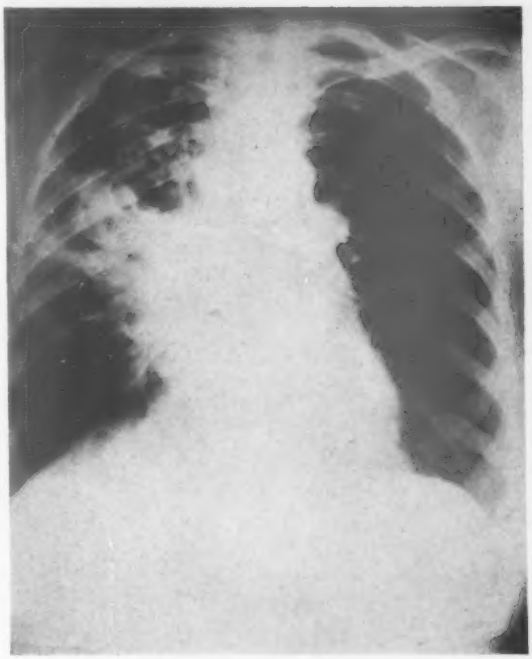

Fig. 12. Case xii. Parenchymal involvement with multilocular cavitation in right upper lobe.

symptoms may result in diagnostic difficulties. Biopsy of accessible material, however, will usually clarify the problem.

III. *Pleural Type*

The pleura contains many small foci of lymphoid cells but no follicles or nodes. Similar lymphoid collections are found in the connective tissue septa separating the secondary lobules. Pleural involvement in Hodgkin's disease is frequent, occurring as nodular or infiltrating masses on the pleural surface. These lesions may produce massive and persistent effusions which can be confused with those of tuberculosis and of carcinoma. The effusions are usually serous in nature although chylous and sanguineous effusions may occur. Pleural effusions may be present in the absence of direct involvement of the pleural surface through pressure by enlarged mediastinal lymph nodes on lymphatic and blood vessels at the hilum.

Case xiii. M. H., white female, aged fifty-two, was admitted because of stiffness and

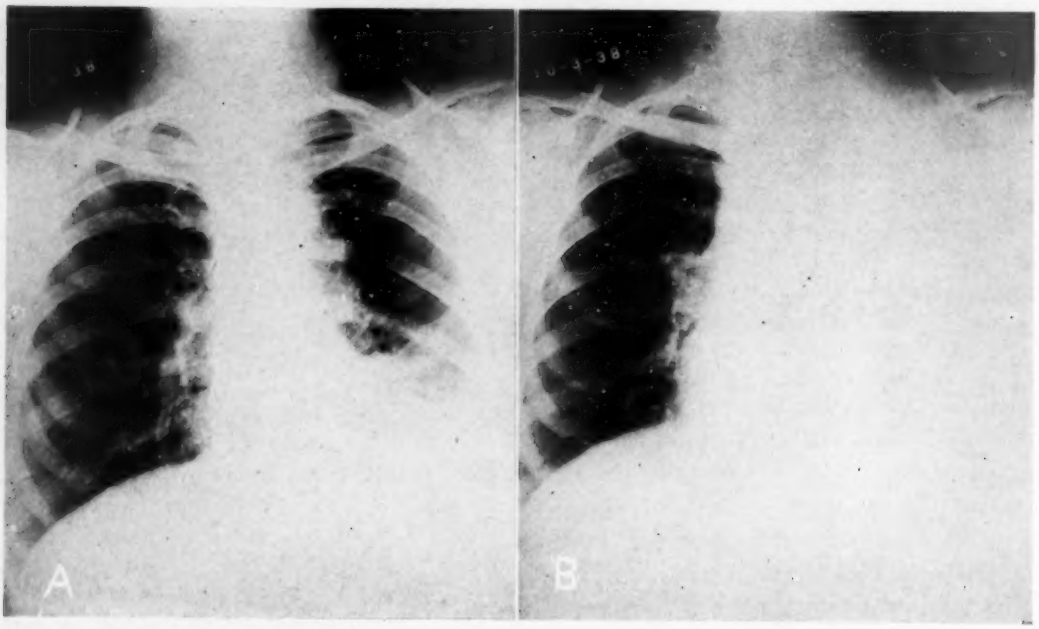


Fig. 13. Case xiii. *A*, pleural involvement in left lower chest. Left hilar nodes involved. *B*, extension of pleural involvment with massive effusion.

swelling of the neck, weight loss of three months' duration, and a sensation of fullness in the throat. Biopsy of a cervical node revealed Hodgkin's disease. The patient showed immediate response to high voltage roentgen therapy, but later died suddenly of pulmonary embolism. Roentgenogram of the chest (Fig. 13*A*) showed early pleural involvement with a small pleural effusion. Later a massive left pleural effusion developed (Fig. 13*B*).

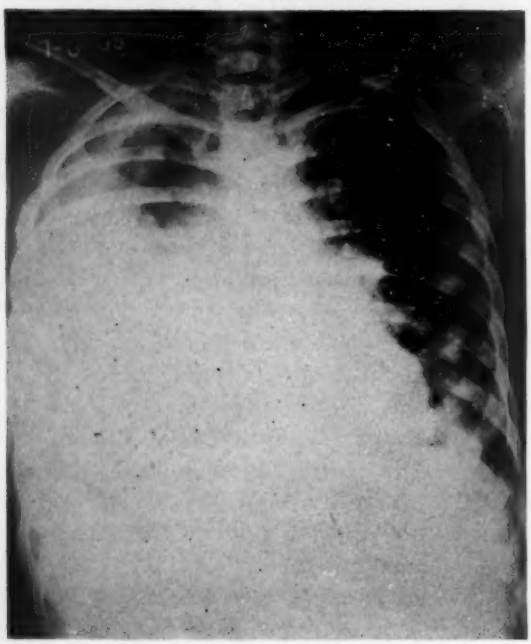

Fig. 14. Case xiv. Extensive right pleural effusion with nodular infiltration in both lungs.

Case xiv. R. K., white male, aged seventeen, was admitted because of enlarged nodes in the left axilla and small nodules in the skin of the right chest wall. Biopsy of the skin lesions showed Hodgkin's disease. Pain developed in the right chest. Later there was cough and shortness of breath. Straw colored serous fluid was aspirated from the right pleural space. There was poor response to irradiation and the patient died one year after the onset of the disease. Roentgenogram of the chest (Fig. 14) showed an extensive right pleural effusion with nodular lesions in both lungs. Autopsy (Dr. E. B. Helwig) revealed generalized Hodgkin's sarcoma. The right and left pleural cavities contained 3,000 cc. and 1,000 cc. of yellow serous fluid respectively. Numerous irregular and somewhat nodular elevated areas measuring from 1 to 4 cm. in diameter were found on the visceral pleurae.

IV. *Osseous Type*

The ribs, sternum and other bony structures may be involved by direct extension of the disease from underlying lymph nodes or granulomatous lung or pleura. Occasionally the process may start in the ribs or sternum and invade the lung.

Case xv. B. R., white male, aged seventeen, was admitted because of generalized pruritus of three months' duration. He had also observed swelling of the upper anterior chest wall during this period. Examination disclosed a mass 7.5 cm. in diameter located in the midline at the level of the junction of the first rib with the sternum. There was no enlargement of the peripheral lymph nodes, liver or spleen. Biopsy of this mass showed the sarcomatous form of Hodgkin's disease. Roentgenograms of the chest and sternum (Fig. 15, *A* and *B*) showed a large mass in the upper right mediastinal region extending anteriorly and causing destruction of the manubrium sterni.

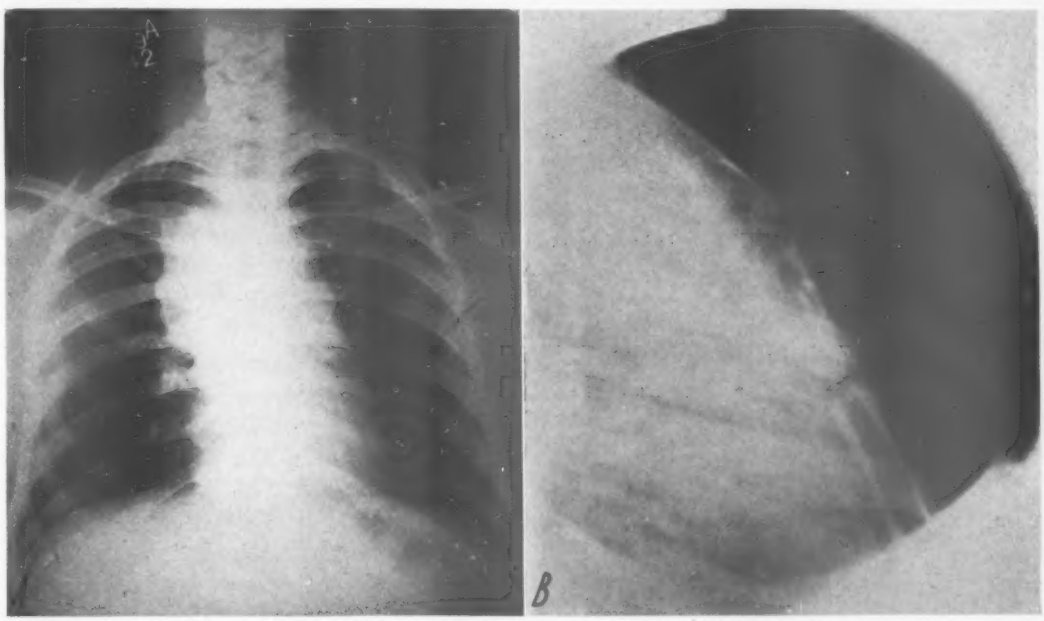

Fig. 15. Case xv. *A*, large upper right mediastinal mass extending anteriorly to involve manubrium sterni. *B*, lateral view of sternum showing destructive process in the manubrium.

V. *Cardiac Type*

The heart is rarely affected in Hodgkin's disease, but may be involved by extension from adjacent structures, particularly the mediastinal lymph nodes. If involved, objective evidence consists of changes in rhythm, the configuration of the heart, and evidences of myocardial insufficiency which may retrogress after therapy. The presence of such evidence during the course of Hodgkin's disease should suggest extension of the process to the heart.

Case iv. B. U., white female, aged twenty-seven, was previously described in this communication. This case was reported in detail by Garvin.[3] In 1938, eight years after the onset of her disease she developed dyspnea on exertion. Roentgenograms of the chest showed an enlargement of the cardiac shadow in its transverse diameter to 16.5 cm. as compared with a previous measurement of 11 cm. Following irradiation to the anterior mediastinum this dimension was reduced to 14 cm. and clinical improvement followed.

One year later she developed congestive cardiac failure with edema, enlargement of the liver and râles at the lung bases. The blood pressure was 100/70. Electrocardiogram showed an inverted $T_2$, low voltage of T and QRS waves

in all leads, and auricular fibrillation. Roentgen therapy to the mediastinum was again administered, as well as digitalis and mercurial diuretics. Marked clinical improvement ensued. The rhythm became normal and the congestive failure disappeared.

She responded well for several months, but returned in June, 1940, with general progression of the disease. She died eighteen months after onset of the cardiac decompensation, and ten years and seven months after the onset of the disease.

At autopsy (Dr. A. E. Margulis), the aorta, the pulmonary arteries, the great veins and the atria were encased in a dense mass of Hodgkin's tissue. The granulomatous tissue invaded the walls of both atria and extended directly into the atrial cavity. The pericardial space was obliterated. Both lungs contained Hodgkin's disease, more particularly the right, the disease extending secondarily from the mediastinum. There was also involvement of the liver, spleen and adrenal glands.

## ROENTGEN THERAPY

Just as roentgen rays have long proved of value in the treatment of Hodgkin's disease of peripheral involvement, radiation therapy has also been useful in the management of Hodgkin's lesions located elsewhere in the body, particularly those involving the thorax. It has been known for many years that the response of mediastinal tumors to small doses of radiation has constituted a differential diagnostic test between the lymphoblastoma group and lesions of different nature. As experience demonstrated the great regularity of retrogressions of mediastinal nodes following the application of roentgen rays, attempts were made by many workers to produce similar results on Hodgkin's lesions involving the thorax. These investigations have been justified, since the results have shown that, while retrogressions cannot be obtained with the same degree of regularity as in the treatment of peripheral lymph node involvement, symptoms in many patients have been relieved and in others the duration of life has been prolonged to a considerable degree. General medical therapy, in conjunction with radiotherapy, is essential if the best results are to be obtained.

Twenty-three of the 35 cases were treated by irradiation. Seventeen cases considered adequately irradiated showed definite favorable response of varying degrees. Three patients with adequate and 2 patients with inadequate dosage showed no favorable response, and in 1 case there was no record of the result of treatment.

Because of the high incidence of involvement of the lymphatic chains of the mediastinum and abdomen found at autopsy, it has become routine in many clinics[6,8] to irradiate these regions in all cases of Hodgkin's disease even though the lesions are not demonstrable by clinical or roentgenological examinations. Jacox, Peirce and Hildreth[8] reported a greater survival rate in those patients who received systemic irradiation to abdominal and mediastinal nodes than in patients who received treatment only to the peripherally involved regions. When the disease is known to exist in the mediastinal and abdominal lymph nodes, larger total doses of roentgen rays are applied to these regions to assure a more certain therapeutic effect.

No definite rules or formulae can be laid down for determining the exact dosage to be applied to all patients, since the irradiation response of lesions varies considerably in different subjects. Instances in our own series range from cases with an extremely high degree of radiosensitivity to only one or two small doses to those which failed to respond in the least to relatively large quantities of roentgen rays. Conventional high voltage apparatus has been employed. The technical factors used were 200 kilovolts, 20 milliamperes, 50, 60 and 70 centimeter target-skin distance and 0.75 mm. Cu plus 2.0 mm. Al filtration (half-value layer of 0.9 mm. Cu). The output in roentgens varied from 35 to 17.5 per minute. The size of the fields ranged from approximately 50 to 150 square centimeters.

In general, for the treatment of mediastinal lymph nodes, it may be stated that 200

r (measured in air) should constitute the average daily dose applied to a lesion and the total dosage over a period of days or weeks should depend upon the response to irradiation from the standpoint of both constitutional and local reactions. The latter can be gauged clinically and by frequent roentgenoscopic or roentgenographic investigations. Some patients may show complete disappearance of their lesions after a few days of treatment while others may require total dosages of 2,000 to 3,000 r directed toward each region involved. For pulmonary lesions, the course may vary from a few daily doses of 300 to 400 r to a longer series of daily doses of 100 r over the affected region utilizing a cross-fire technique of anterior, posterior and lateral fields where possible. The total dosage to each field in the latter procedure should be at least 1,000 r. Good temporary retrogressions have been observed in 2 cases treated through anterior and posterior fields without the occurrence of undue irradiation sickness.

Single massive doses (500 to 600 r) are avoided because of undesirable constitutional effects and greater damage to normal tissues which might require more treatment at a later date should recurrence take place. However, Craver[2] states, in referring to Hodgkin's disease in general, that fewer, but larger single doses have proved to be of as much benefit, if not more, than divided doses administered in larger total quantities. It is evident from a review of the literature that no consensus has been arrived at regarding dosage technique.

SUMMARY

Of 55 proved cases of Hodgkin's disease in which chest roentgenograms were available, 35, or 63 per cent, showed intrathoracic involvement. The varied manifestations of intrathoracic Hodgkin's disease were correlated with the distribution of lymphoid tissue within the chest. Mediastinal, parenchymal, pleural, osseous and cardiac types were described and illustrated by 15 case reports.

Roentgen therapy was discussed and it was concluded that the majority of patients with intrathoracic Hodgkin's disease will show definite but varying degrees of favorable response to roentgen treatment.

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# SOME ROENTGENOLOGICAL AND PATHOLOGICAL ASPECTS OF CALCIFICATION OF THE CHOROID PLEXUS*

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A REVIEW of some of the established facts regarding the histopathological changes which result in choroid plexus calcification has been undertaken with the hope that we might be better able to evaluate the significance of the shadows cast in the roentgenogram and to appraise their value in the diagnosis of expanding intracranial lesions. Our interest in this subject has been aroused by several cases of aberrant choroid plexus calcification and the problems introduced in deciding their importance. Two cases of choroid plexus calcification occurring at ages earlier than any yet reported were encountered.

## HISTORICAL

Herophilus and his associates were probably the first investigators to gain substantial knowledge of the human choroid plexuses, as a result of anatomical studies at the ancient University in Alexandria. From Galen[26] we learn that Herophilus investigated the minor tortuosities of the cerebral meninges, to which he applied the appropriate name chorioid (chorion-like) because of their resemblance to the fetal membranes. Galen,[27] himself, was impressed by their resemblance to this fetal structure.

## ANATOMICAL DISCUSSION

The development of the choroid plexuses of the lateral ventricles in the human embryo has been traced by Bailey[2] from an area in the lateral roof plate of the telencephalon. The tela choroidea superior and tela choroidea inferior arise through a mesenchymal overgrowth and vascularization of the roof plates of the third and fourth ventricles. Here the choroid plexuses are formed by an invagination of the roof epithelium by the development of plexus tissue in the overlying pia-arachnoid.

In the fully developed brain the choroid plexuses of the lateral ventricles are highly vascular folds of pia-arachnoid which project into the ventricular cavities. They extend from the ends of the temporal horns to unite at the interventricular foramina described by Monro[40] through which they pass into the tela choroidea of the third ventricle. Here the plexuses continue as a pair of narrow paramedian bands of plexus tissue extending from the interventricular foramina to the suprapineal recess. Two highly vascular invaginations of the tela choroidea inferior constitute the choroid plexuses of the fourth ventricle. The horizontal portions of each are joined to form a continuous band extending from one lateral recess to the other, while the vertical portions branch at right angles from the horizontal and extend toward the obex on each side of the midline.

The choroid plexuses are covered by a simple layer of cuboidal ependymal cells which everywhere separates the mesenchymal elements from the ventricular cavities. Beneath the villi the stroma is composed of delicate white fibrous tissue which is gathered together into bundles or trabeculae which form a network with numerous spaces of all shapes. These spaces are lined throughout by a single layer of flattened cells. The choroid plexus in the atrium of each lateral ventricle is expanded to form a fusiform swelling known as the glomus. This expansion is brought about to a large extent by an increase in number and size of the pia-arachnoid cavities, somewhat analogous to the subarachnoid cisterns.

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The function of the choroid plexuses is the production of the cerebrospinal fluid contained in the ventricles of the brain. The evidence for this belief has been reviewed by Weed.[59] There is fairly general agreement that under normal conditions the choroid plexuses have no resorptive function. The findings of Foley[24] and Hassin[29] led them to believe that under certain circumstances they could assume such a function. The work of Wislocki and Putnam[61] and of Dandy and Blackfan,[13] however, discredits this opinion.

## PATHOLOGICAL PROCESSES IN THE CHOROID PLEXUSES

It has been pointed out by Beals[3] how few pathological processes, aside from tumors, have been ascribed to the choroid plexuses. The experiences of Cushing[11] and Davis and Cushing,[14] Elsberg,[20] Tooth,[54] Liber and Lisa,[35] and others, show that even tumors of choroid plexus origin are uncommon. Gamgee,[28] Ziegler,[63] and Manlove and McLean[39] described the occurrence of cholesteatomas of the choroid plexuses in horses and in man.

The formation of cysts and psammoma bodies in the choroid plexuses are generally considered to be regressive changes of such common occurrence that they are of negligible pathological significance. According to Findlay,[23] Hooper[31] first described the cystic changes. They were beautifully illustrated in colored drawings by Luschka.[38]

Psammoma bodies occur in all of the membranes of the brain and spinal cord and are also commonly present in tumors arising in these membranes. Some of the earliest descriptions of these bodies were given by Hooper,[31] Bergmann,[4] and Remak,[45] although Bergmann stated that they were known before this time. The calcified bodies have been variously named psammoma bodies, corpora arenacea, corpora amylacea, calcospherites, concentric concretions, acervulus cerebri, brain sand and sabulous bodies. Virchow[57] attempted to differentiate by iodine staining between the corpora amylacea which are commonly found in the brain substance and the calcified structures of the choroid plexuses and meninges which he called psammoma bodies. This differentiation subsequently has been extended as it has been shown by Lafora,[34] Ferraro and Damon,[21] and others, that the corpora amylacea of the brain are probably of microglial or oligodendroglial origin while the psammoma bodies are formed quite differently.

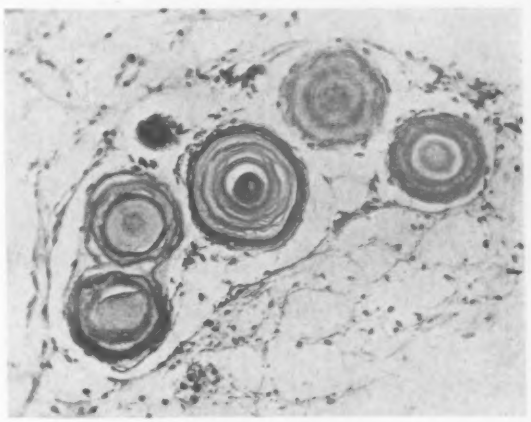

Fig. 1. Psammoma bodies in the connective tissue stroma of a choroid plexus of a fifty-six year old man. The usual concentric lamination of the bodies is shown. Two conjoined masses are shown in the lower left corner. (Hematoxylin and eosin stain × 320.)

Von Zalka[62] and Biondi[5] have shown that the changes of deterioration which occur in the choroid plexuses are found with considerable frequency after the age of forty, generally corresponding to the age of onset of regressive brain changes as shown by Boyd.[6] The calcified bodies occur in all regions of the plexuses in the stroma or pia-arachnoid portion (Fig. 1). They vary greatly in number and size and according to Karsner[33] they may measure up to 3 mm. in diameter. For the most part they appear as rounded bodies made up of concentric rings. Conjoined or aggregated masses of such bodies are frequently found enclosed in a single fibrous envelope. It is thought by many that the ground substance of the corpora arenacea or psammoma bodies is a structureless matrix in which calcium salts

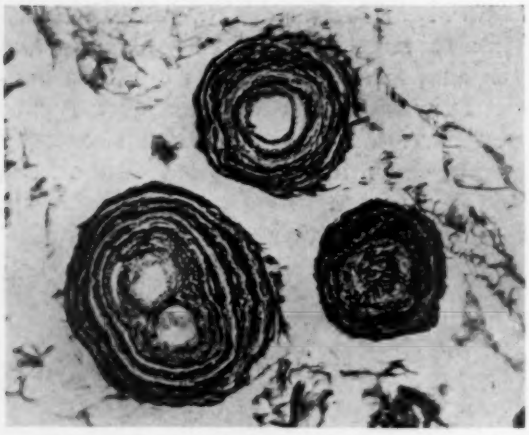

Fig. 2. The framework of the psammoma bodies is shown to be composed of dense collagen and argyrophilic reticular fibers in which calcium salts become deposited. Some of the fibers are arranged in dense concentric layers while others run irregularly in all directions. (Laidlaw's silver stain × 400.)

become deposited and some authors have described them as structureless aside from concentric markings. Silver stains, however, show that even the well calcified psammoma bodies have an intricate framework of closely packed fibrous reticulum (Fig. 2).

The mechanism of formation of psammoma bodies has long been a subject of debate. Virchow[58] was convinced that the bodies originated chiefly through a proliferation and stratification of cells within

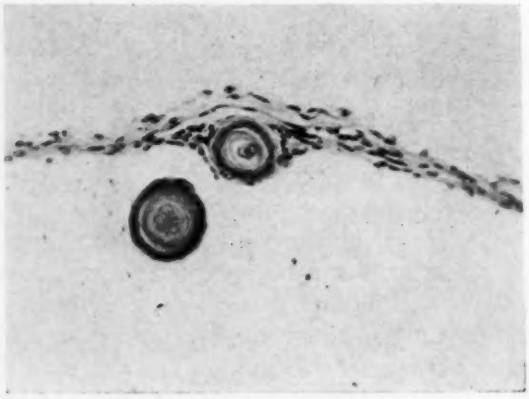

Fig. 3. A concentric body has formed in the wall of a small cyst of a choroid plexus. Another lies free in the cyst. (Hematoxylin and eosin stain × 470.)

the connective tissue of the plexuses which became the seat of a process of petrification. The thorough studies of Findlay[22,23] led him to a rather similar conclusion. Cushing and Weed[12] studied the calcareous deposits of the arachnoid and found that calcification starts in the nuclei of the degenerating groups of cells at an early stage of the process. Rokitansky,[46] Findlay,[23] and von Zalka[62] showed that many of the calcifications may arise in cysts of the plexuses (Fig. 3). Taft[53] and others believed that the underlying pathological process is a fibrous obliteration of the vessels of the villous tufts, with resultant hyaline changes in the tips of the tufts or the formation of

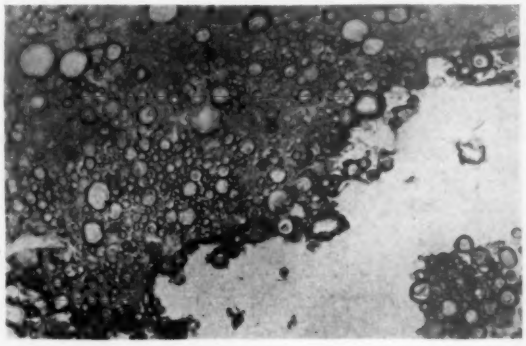

Fig. 4. Myriads of tiny concentric bodies are shown entering into the formation of a calcium mass which grossly appeared as a small fleck of calcium 1.5 mm. in length and 0.5 mm. in diameter. This formed part of the choroid calcification found in Case v. (Hematoxylin and eosin stain × 400.)

cysts, while Cornil and Ranvier,[10] Findlay,[23] and Biondi[5] believed that the choroid calcification may sometimes arise in the vascular segments themselves.

The formation of bone in the choroid plexuses has been described by Findlay[23] and Sachs and Whitney.[48] Wells[60] and Asami and Dock[1] have pointed out that any area of calcification is likely to be replaced by bone, regardless of the tissue involved, through a stimulation of connective tissue to form bone. For the most part it appears that the congregation of multitudes of psammoma bodies in the expanded glomus to form a conglomerate calcium

mass accounts for the shadows most commonly cast in the roentgenograms as in Case v (Fig. 4).

### ROENTGENOGRAPHIC DEMONSTRATION OF CHOROID PLEXUS CALCIFICATION

Schüller[49] was the first to mention the roentgenographic demonstration of choroid plexus calcification. Heuer and Dandy,[30] Ström[52] and O'Sullivan[43] later described similar calcification and pointed out its bilateral occurrence. Camp[7,8] has emphasized the importance of recognizing choroid plexus calcification and differentiating it

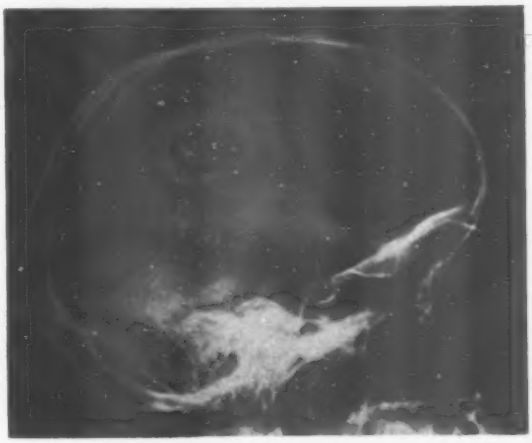

Fig. 5. Punctate calcium shadows in the choroid plexuses which have been described as resembling a collection of tiny glass beads.

from a displaced calcified pineal gland or a tumor. The work of Dyke, Davidoff and Elsberg[18,19] has enabled us to recognize the choroid plexuses by encephalography and ventriculography in a large percentage of cases and to localize calcium shadows in them with a high degree of certainty.

The incidence of choroid calcification recognizable by roentgen examination has been variously given. In a large series Dyke[15] found that 5.1 per cent showed choroid calcification. Childe[9] reported that 11.2 per cent of 1,000 cases showed calcification of the choroid plexuses while Schwartz[50] described a 13 per cent incidence. The percentage found is greatly increased if cases below twenty years of age

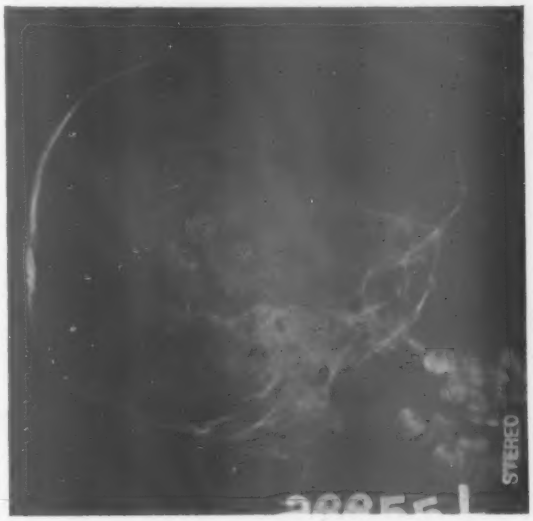


Fig. 6. Bilateral calcification in the glomera of the choroid plexuses of the lateral ventricles of the form which has been likened to a popped kernel of corn.

are excluded. Beals[3] found that 28 per cent of a group over twenty years of age showed such calcification.

The calcification may assume different forms on the roentgenograms. A common form is a collection of punctate shadows which Camp[8] likened to a cluster of tiny glass beads (Fig. 5). Dyke and Davidoff[18] described forms which they thought resembled a popped kernel of corn (Fig. 6). In other cases the shadows appear linear and crescentic (Fig. 14). In many instances they are a combination of several forms or appear as irregular amorphous solid masses of calcium.

Most authors have emphasized the symmetry of the calcification occurring in the plexuses. Beals,[3] Lowman and von Storch,[37] Vastine,[55] and others, have stated that the two shadows of the calcified choroid glomera and the pineal shadow can be considered as being located at the angles of an isosceles triangle formed by drawing lines between these shadows on the anteroposterior or posteroanterior skull roentgenogram. Although the calcification is usually fairly symmetrical it may vary considerably in extent and density on the two sides. Jacobsson[32] has pointed out the importance

Fig. 7. Asymmetrical calcification of the choroid plexuses. The roentgenograms were made in the course of study of a case of thyroid disease. (Same case as Figure 6.)

of recognizing that an asymmetrical distribution of calcium is encountered in some cases (Fig. 7). Calcification may even be unilateral. The position of the glomera may vary due to atrophy or hypoplasia of one cerebral hemisphere. Since psammoma bodies can occur in all portions of the plexuses it is reasonable to assume that occasionally they may attain sizable proportions elsewhere than in the glomera.

### CHOROID PLEXUS CALCIFICATION IN CHILDREN

Calcification of the choroid plexuses may occasionally occur at an early age. Rothstein[47] described such calcification in a child four years of age. The following two cases illustrate calcification of the choroid plexuses in still younger children and in unusual locations.

Case I (N.I. No. 18326). F. R., male, aged two and a half years. The patient was admitted December 18, 1933, because of convulsions which began at the age of ten months, and which were of increasing frequency. He was born after a prolonged labor but appeared to develop normally until the age of ten months. At this time he began to have convulsions and developed a left hemiplegia. Development was markedly retarded. The child was unable to sit, walk or talk and was apathetic to his surroundings. Blood examination disclosed a slight hypochromic anemia.

Roentgen examination of the skull showed no evidence of increased intracranial pressure. There was calcification in the glomus of the choroid plexus of each lateral ventricle and a calcium shadow, just to the right of the midline, was projected through the region of the pterion. Encephalograms revealed a generalized enlargement of the ventricular system and verified the presence of calcification in the choroid glomera. The anterior calcium shadow appeared to be in the anterior pattern of the plexus tissue near the interventricular foramina.

The diagnosis of cerebral spastic infantile paralysis was made clinically. The patient's behavior was that of an idiot and he was unimproved during his stay in the hospital.

Case II (N. I. No. 14030). B. B., female, aged three years. The child was admitted October 18, 1943, because of convulsions beginning at the age of three months, and retarded development. She was born following a normal term delivery. On admission the child was found to be mentally deficient and unable to talk. There was generalized muscular hypotonicity and an ataxia.

Encephalograms showed the lateral and fourth ventricles to be normal in shape and position but slightly enlarged. The cisternae

Fig. 8. Case I. Bilateral calcification in the glomera of the choroid plexuses of a child, aged two and a half, with calcification in the region of the interventricular foramina.

pontis and magna were also rather large. Several calcified masses were present in the choroid plexuses of the lateral ventricles. One shadow was just to the left of the midline at the interventricular foramina, one was in the mid-portion of the body of the right lateral ventricle and one was present in each glomus.

A diagnosis of cerebral and cerebellar aplasia was made. The patient's course was stationary during her hospital stay and she was discharged to enter a sanatorium for permanent institutional care.

*Discussion.* Case I (Fig. 8 and 9) and Case II (Fig. 10) illustrate aberrant calcification in the choroid plexuses of very young children. In one instance calcification was present in the choroid plexus in the body of a lateral ventricle while in both cases calcification occurred in the choroid glomera and at the interventricular foramina.

### CALCIFICATION IN THE REGION OF THE FOURTH VENTRICLE

Calcification of the choroid plexuses of the fourth ventricle has not been described in the literature to our knowledge. Jacobsson[32] was also unable to find a report of such a case. In the following instance calcification was found in the posterior fossa in the region of the fourth ventricle.

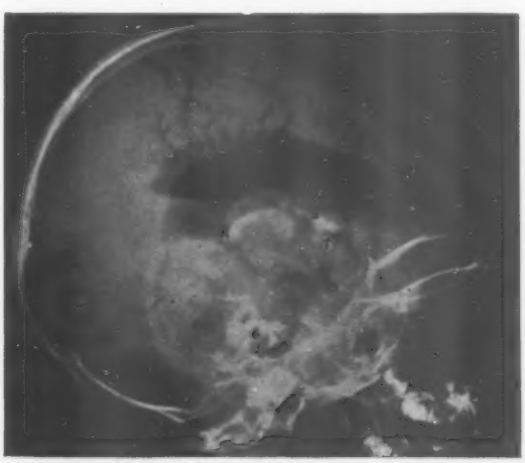

Fig. 9. Case I. Encephalogram showing the posterior calcium shadows to be in the choroid glomera. The anterior calcification appears to be in the plexus tissue near the interventricular foramina.

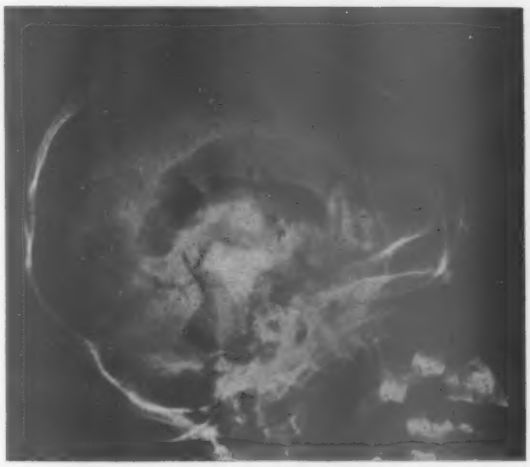

Fig. 10. Case II. Encephalogram of a child, aged three, showing bilateral calcification in the choroid glomera. There are rounded shadows of calcium density which appear to be due to choroid calcification in the mid-portion of the body of the right lateral ventricle and near the interventricular foramina.

Case III (N. I. No. 33113). A. W., male, aged fifty-three. The patient was admitted April 25, 1937, because of severe headaches and mental confusion of three hours' duration. He had been in good health aside from mild headaches which had occurred for many years. On the day of admission he had a sudden onset of severe headache followed by a severe backache and mental confusion. There was no loss of consciousness or convulsion. On admission the blood pressure was 146 systolic and 100 diastolic. The heart was not enlarged. There was a slight lower right facial weakness. Deep tendon reflexes were generally slightly hyperactive. Speech was slow and rather indistinct. Ophthalmological examination was negative. The cerebrospinal fluid contained 2.08 million red blood cells per cu. mm. and there was 433 mg. of total protein per 100 cc.

Roentgen examination of the skull was negative except for a punctate shadow of calcium density in the posterior fossa near the midline in the region of the fourth ventricle. A diagnosis of subarachnoid hemorrhage of unknown origin was made. The patient became clear mentally and the facial weakness, increased reflex activity and speech defect disappeared during the five weeks' hospital stay.

On March 31, 1943, six years after the first examination, the patient was in good health

with no complaints except for occasional headaches which were promptly relieved by aspirin. Roentgenograms of the skull showed no change in the punctate shadow in the region of the fourth ventricle previously described.

*Discussion.* Choroid calcification is apparently very rarely demonstrated by roentgen methods in the fourth ventricle in contrast to the frequency with which it is found histologically. Virchow[58] long ago pointed out that the psammoma formations are "an everyday occurrence in the region of the medulla oblongata where they appear in the nipple of choroid plexus on the roof of the fourth ventricle" (Fig. 11). Case III (Fig. 12 and 13) showed roentgen evidence of a punctate calcium mass in the posterior fossa in this region. Laminagrams showing this shadow to be located in the mid-sagittal plane aided in differentiating it from pathological calcification in the cerebellum. The shadow has remained unchanged over a six year period of observation.

Fig. 11. Psammoma bodies in a choroid tuft of the fourth ventricle (after Virchow).

### Displacement of Choroid Plexus Shadows by Expanding Intracranial Lesions

The use of physiologically calcified intracranial structures, especially the calcified pineal gland, as landmarks in the diagnosis of brain tumors has been described by Naffziger,[41] Vastine and Kinney,[56] Dyke,[15] Lilja,[36] and others. Newell[42] mentioned displacement of a calcified choroid glomus as an aid in the diagnosis of brain tumor but failed to report the case in the literature. Eight years later Lowman and von Storch[37] formally reported for the first time such pathological displacement. Fray,[25] Childe,[9] Pancoast, Pendergrass

Fig. 12. Case III. A punctate shadow of calcification in the posterior fossa of a man, aged fifty-three, in the region of the fourth ventricle. It has remained unchanged for six years. The pineal is also calcified.

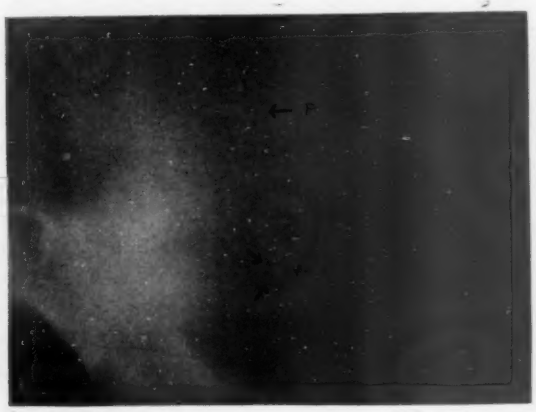

Fig. 13. Case III. A mid-sagittal laminagram showing the punctate calcium shadow to be near the midline.

and Schaeffer,[44] Dyke,[17] and Jacobsson[32] have subsequently described displacement of a glomus by expanding intracranial lesions. Most of the lesions which have been reported as causing displacement of the calcified choroid glomus have been tumors posterior to the glomus or in the temporal lobe, causing forward, upward or medial displacement, or any combination of these three, as emphasized by Fray[25] and Childe.[9]

Displacement of one calcified choroid glomus is occasionally the only evidence on the plain skull roentgenograms of an expanding intracranial lesion. This occurred in the following 2 instances.

Case iv (N. I. No. 13276). J. R., male, aged fifty-five, an American printer, was admitted July 27, 1943, because of headaches and failing vision which he had had for one month. He was asymptomatic until one month before admission when he developed severe headaches, failing memory and vision, and dizziness. He was unable to think of words or to express his thoughts. He showed mental confusion, ataxia and a tendency to fall backward to the right. There was a slight increase in deep tendon reflexes on the right and a right homonymous hemianopsia. Papilledema was present, more marked on the left.

Roentgen examination of the skull was negative except for the abnormal anterior position of the calcification in the left choroid glomus. The pineal was calcified and was in its normal position. Attempted ventriculograms revealed

Fig. 14. Case iv. Anterior displacement of the calcified left choroid glomus by a tumor.

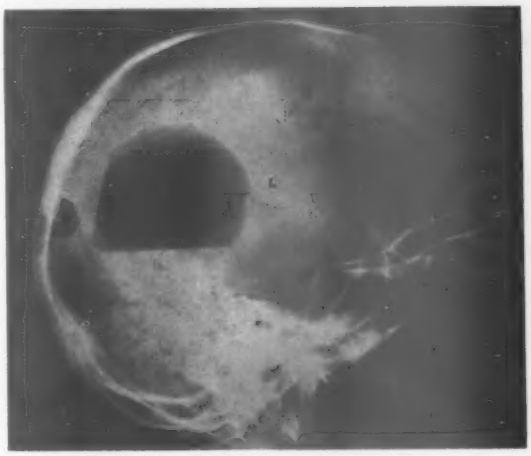

Fig. 15. Case iv. Attempted ventriculogram showing a large gas-filled cyst in the left posterior parietal and occipital regions.

a globular gas-filled cyst in the left occipital region which was interpreted as a cystic tumor. There was no filling of the ventricular system.

At operation a solid and cystic tumor was found in the left occipital region. Histopathological examination of the surgical specimen revealed it to be a metastatic carcinoma of unknown origin.

Case v (N. I. No. 16244) G. D., male, aged fifty-seven, an English mechanic, was admitted June 3, 1933, complaining of loss of memory and difficulty in walking of two years' duration. During this same time he had suffered a personality change. Equilibratory tests were poor. An increase in deep tendon reflexes and a Babinski sign were present on the right side. The patient was mentally deteriorated. The cerebrospinal fluid contained 283 and 4864 red blood cells per cu. mm. on two examinations and the total protein was 100 mg. per 100 cc.

Skull roentgenograms showed the calcification in the left choroid glomus to be higher and more posterior than usual. The sella turcica and posterior clinoid processes appeared normal and the calcified pineal gland was in its normal position.

On the thirteenth hospital day the patient developed fever and physical signs suggestive of consolidation in the left lung. He became progressively worse and died on the seventeenth hospital day. At necropsy (Presbyterian Hospital Autopsy No. 11272) a walnut-sized aneurysm of the basilar artery was found located 1 cm. anterior to its formation from the vertebral

Fig. 16. Case v. Unusual upward and backward displacement of the calcified left choroid glomus by an aneurysm of the basilar artery.

arteries. Two-thirds of its bulk lay to the left of the midline. The wall of the aneurysm was grossly intact. A bilateral lobular pneumonia was present.

*Discussion.* The more common type of anterior displacement of one calcified choroid glomus by a cerebral tumor is illustrated by Case iv (Fig. 14 and 15). An unusual occurrence of upward and backward displacement by an aneurysm of the basilar artery was present in Case v (Fig. 16 and 17). The displaced calcified glomus is of interest as a diagnostic aid in Case v since the basilar artery lesions do not usually show the roentgen changes described by Sosman and Vogt[51] and Dyke[16] as common features of internal carotid artery aneurysms.

## COMMENT

Disturbance of the usual triangular relationship of the calcified choroid plexuses and calcified pineal gland has been considered evidence of displacement by an expanding intracranial lesion. Varying degrees of asymmetry may be observed in the absence of organic disease or in the presence of hypoplasia or atrophy of one cerebral hemisphere. The view of Jacobsson[32] that asymmetrical calcification in the choroid plexuses does not in itself permit the conclusion that an expanding intracranial lesion is present seems well founded, unless such asymmetry is gross. In the majority

Fig. 17. Case v.

of cases observed at the Neurological Institute in New York in which the plain skull roentgenograms have revealed a definite displacement of one calcified choroid glomus other evidence of an expanding intracranial lesion has also been present.

## SUMMARY

1. Calcification occurs in the choroid plexuses probably for the most part through a process of proliferation of cells of the pia-arachnoid followed by the formation of a dense collagenous and fibrous reticular meshwork in which calcium salts become deposited.

2. Calcification occurring in the glomera of the choroid plexuses in the lateral ventricles assumes various forms and is frequently asymmetrical.

3. Two cases are described in which roentgenographically demonstrable choroid plexus calcification occurred in unusual positions and at very early ages (two and one-half and three years).

4. One case exhibiting punctate calcification in the region of the fourth ventricle is reported.

5. Two cases are reported in which a displaced calcified choroid glomus was the only evidence on the plain skull roentgenograms of an expanding intracranial lesion.

6. An unusual case of upward and backward displacement of the glomus of a choroid plexus by an aneurysm of the basilar artery is described.

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VOL. 52, NO. 4

# PARASTERNAL DIAPHRAGMATIC HERNIA*

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DIAPHRAGMATIC hernia was considered a surgical curiosity which could be diagnosed only at operation or the autopsy table until but a comparatively few years ago. During the past decade, however, this condition has been recognized with ever increasing frequency until it is now generally accepted by clinicians as a relatively common cause of upper abdominal and chest complaints. Due to rapid improvements in roentgen techniques and diagnostic methods, the varied manifestations and great clinical importance of these hernias are becoming more widely understood and appreciated. The tremendous increase in the numbers of cases of diaphragmatic hernia of various types appearing both in the roentgenologic literature and other medical journals is not due to an actual increase in incidence, but rather to the fact that both clinicians and roentgenologists now realize that a hernia may be present in every case presenting atypical, recurrent or persistent upper abdominal and thoracic complaints; and along with this increasing awareness, more thorough search is made for this condition in all obscure cases. Many patients have been saved from exploratory operation or prolonged treatment for neurosis and other incorrectly diagnosed conditions by the roentgen demonstration of a diaphragmatic hernia which adequately explained the bizarre symptomatology.

Diaphragmatic hernia is defined as the protrusion of any abdominal viscus into the thoracic cavity through an opening in the diaphragm. The defect may be the result of imperfect development, anatomic weakness, or trauma, and may be either congenital or acquired. Practically every organ of the abdomen and pelvis except the rectum, bladder and genitalia has been reported as occurring in hernia. Hernias involving the diaphragm always take place in an upward direction because of the pressure relationship on the two sides of the diaphragm, there being a positive pressure in the abdominal cavity while a negative pressure is normally present in the thorax.

There are numerous types of diaphragmatic hernia and the classification of these lesions is difficult and not yet entirely satisfactory. This is due to the fact that previous writers have used different systems of nomenclature and various methods of classification. However, the following is suggested because of its simplicity and comprehensiveness:

A. Non-traumatic
   1. Congenital (due to embryonic defect)
      a. Esophageal hiatus
      b. Pleuroperitoneal foramen of Bochdalek
      c. Dome of diaphragm
      d. Foramen of Morgagni
      e. Absence of a portion of the diaphragm
   2. Acquired
      a. Esophageal hiatus
      b. Pleuroperitoneal foramen
      c. Foramen of Morgagni

B. Traumatic
   1. Blows to abdomen
   2. Penetrating wounds
   3. Perforation of subphrenic abscess or empyema

A brief review of the anatomy will assist in clarifying the pathogenesis of the various types of hernia. The diaphragm is a dome-shaped, musculofibrous septum which serves to divide the thoracic and abdominal cavities. It is composed of three groups of muscular fibers which originate peripherally from the circumference of the thorax and converge to be inserted into a central tendon. The muscular portions are grouped as follows: (1) the sternal part

* Read at the meeting of the New England Roentgen Ray Society, Boston, Mass., April 23, 1943.

Fig. 1*A*. Parasternal diaphragmatic hernia. May 21, 1934. Female, aged sixty-four. She has 3 children living and well. Patient entered the hospital complaining of rectal bleeding of five years' duration. Also has gas on stomach, aggravated by eating. Hysterectomy performed thirteen years previously. Barium enema studies reveal a parasternal diaphragmatic hernia and colitis. Roentgenogram of the chest shows a rounded area of mottled density in the right lower lung field. The heart shadow is displaced slightly to the left. The loop of bowel in the thoracic cavity contains gas, producing an area of increased radiance in the paravertebral portion of the right middle and lower lung field.

arising from the posterior surface of the tip of the sternum; (2) the costal portion, originating from the medial surface of the cartilages and the six lower ribs on each side, and (3) the lumbar part, which arises from the lumbocostal arches and crura.

The diaphragm is pierced by three large openings—the aortic, the esophageal, and the vena caval. The aortic hiatus lies slightly to the left of the midline and just anterior to the first lumbar vertebra. The esophageal hiatus is at the level of the tenth dorsal vertebra and is above, in front, and to the left of the aortic hiatus. The vena caval foramen lies at the level of the fibrocartilage between the eighth and ninth dorsal vertebrae and is anterior and to the right of the esophageal hiatus. Failure of fusion of the costal and lumbar portions of the diaphragm results in a persistent pleuroperitoneal hiatus or foramen of Bochdalek. Lack of fusion of the sternal and costal portions forms the so-called foramen of Morgagni with development of the parasternal diaphragmatic hernia, in which we are particularly interested in the present discussion.

However, even under normal conditions, the so-called Larrey's spaces, which correspond anatomically to the site of the foramen of Morgagni, form congenitally weak areas in the diaphragm which may predispose to herniation. These spaces are

Fig. 1*B*. Same as Figure 1*A*, lateral projection. May 21, 1934. The rounded density at the right base lies well anteriorly, the characteristic picture in parasternal diaphragmatic hernia. The gas-containing loop of bowel is seen in the anterior and superior portions of the mass in the right lower lung field.

small, bilaterally symmetrical triangles delimited anteriorly by the sternum, medially by the sternal portion of the diaphragm, and laterally by the costal portion of the diaphragm in the region of its attachment to the seventh costal cartilage. They lie with their apices directed toward the central tendon of the diaphragm and their bases at the costal margins adjacent to the xiphoid. Deficiencies in the diaphragmatic musculature are normally present in these triangles, the spaces being occupied by areolar and connective tissue with a covering of pleura and pericardium superiorly and peritoneum inferiorly. In some instances, the sternal attachment of the diaphragm is entirely absent and the two triangles of Larrey fuse into a single large defect behind the sternum and costochondral junctions with the formation of a large opening through which herniation may readily occur.

Morgagni first recorded a case of hernia through the right side of the diaphragm anteriorly in 1769. The number of reported cases remains extremely small, however. During the years 1930–1941, Harrington[1] states that only 24 cases of parasternal diaphragmatic hernia were reported. Morton[2] in 1939 found a total of 120 cases of parasternal hernia recorded in the literature. Their rarity makes them of particular interest and also stresses the importance of a clear and thorough understanding of their manifestations lest they be diagnosed incorrectly or overlooked entirely. It is our impression that cases of parasternal diaphragmatic hernia have frequently been misinterpreted as thoracic neoplasms and that there are actually many more cases in existence than the number of recorded cases leads one to believe. Of particular significance in this respect is the fact that

Fig. 1*C*. Same as Figures 1*A* and 1*B*. January 24, 1941. Barium enema studies, posteroanterior projection. The herniated loop of bowel is filled partially with barium mixture and partially with air. There is upward and medialward displacement of the cecum and ascending colon.

Fig. 1*D*. Same as Figures 1*A*, 1*B*, and 1*C*. January 24, 1941. Opaque enema, lateral projection. The barium filled colon loop above the diaphragm lies well anteriorly, the greater portion of the mass being made up of soft tissues (omentum, etc.). This patient was under observation for almost seven years with no demonstrable change in the hernia.

Fig. 2*A*. Parasternal diaphragmatic hernia. January 11, 1941. Female, white, married, aged sixty-five. Patient stated she had 21 pregnancies and has 12 living children. For several years, she has suffered with gas, indigestion, and pain in the abdomen and lower back. Six weeks prior to admission, she developed marked anorexia and nausea with dyspnea on exertion. Opaque enema studies show a portion of the transverse colon lying in the thoracic cavity, the pathognomonic finding in parasternal diaphragmatic hernia.

in many instances the condition presents a characteristic roentgen appearance and the diagnosis can be established by roentgenography and roentgenoscopy of the thorax.

We shall attempt in this brief discussion to stress the salient features of the roentgen findings which should direct the observer's attention to the possibility of the presence of this condition and enable him to establish a positive diagnosis of a parasternal herniation. We have made the diagnosis in 6 instances, the majority of the cases having been first demonstrated by roentgenography of the chest and definitely confirmed by studies of the gastrointestinal tract. Since the protrusion of the abdominal organs into the right chest cavity is apt to interfere with expansion of the inferior portions of the lungs and disturb respiratory activity, the clinician focuses his attention on the chest. Likewise, as the hernia produces a shadow at the base of the lung, the roentgenologist is prone to consider that he is dealing with a pulmonary neoplasm and fails to diagnose the real cause of the condition unless he is alert to the possibility of a parasternal hernia.

It is not universally agreed whether these hernias are congenital or acquired. However, they are doubtless on a fundamental biologic basis and are herniations either through a congenital defect in the diaphragm or the result of faulty attachment of the diaphragm anteriorly. There is usually a peritoneal covering, as proved both by autopsy and at operation, indicating that the peritoneum had been completely formed and had closed off the abdominal cavity from the pleural space before the hernia had developed. It is not possible to explain the occurrence of this

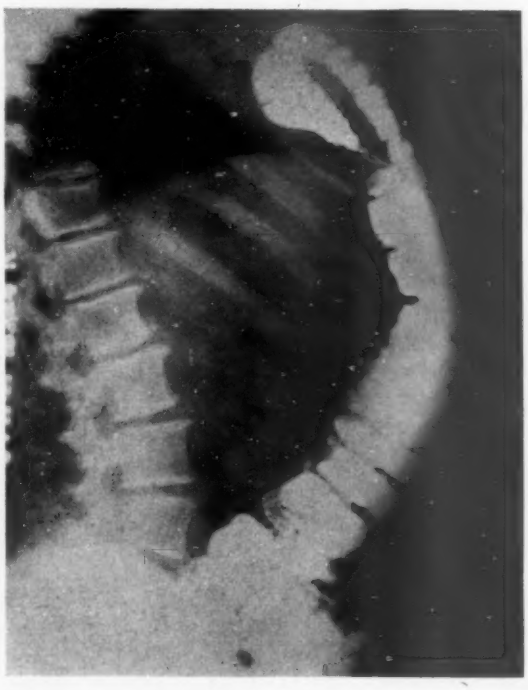

Fig. 2*B*. Same as Figure 2*A*. Opaque enema, lateral projection, illustrating that the herniated loop of colon does not comprise the entire chest mass.

lesion on the basis of faulty fusion or malformation of the various components of the diaphragm. The round and falciform ligaments of the liver are usually found in the peritoneum forming the sac, indicating that there is a relationship between the occurrence of the abnormal opening in the diaphragm and the rotation of the liver into the right side of the abdomen during embryonic development. These hernias occur more frequently on the right side because of the more extensive attachment of the pericardium to the left anterior chest than to the right.

As previously mentioned, the incidence of parasternal hernias is very low and they are among the least frequently diagnosed diaphragmatic hernias. The Mayo Clinic[1] figures on the relative incidence were as follows:

| | Cases |
|---|---|
| Hiatus type | 217 |
| Traumatic | 40 |
| Congenital defect | 5 |
| Foramen of Bochdalek | 4 |
| Foramen of Morgagni | 4 |

Fig. 2*C*. Same as Figures 2*A* and 2*B*. Lateral view of the chest, demonstrating the mass in the antero-inferior portion of the chest.

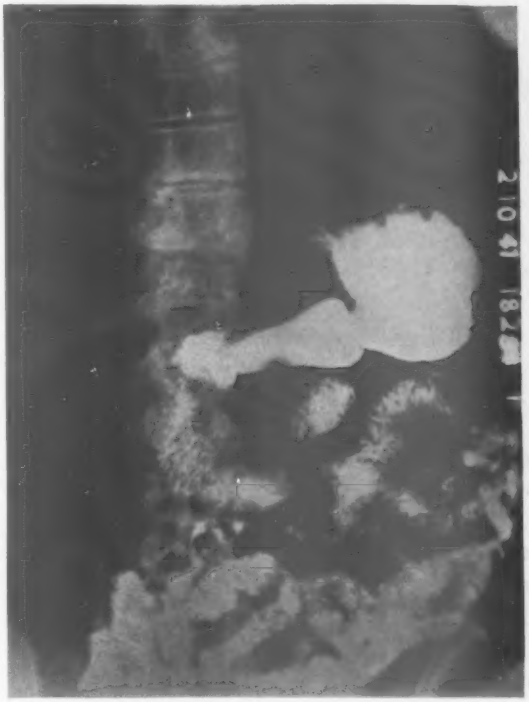

Fig. 2*D*. Same as Figures 2*A*, 2*B*, and 2*C*. Roentgenogram of the stomach, duodenum, and proximal loops of small intestine, revealing that these portions of the intestinal tract are not involved in the hernia.

In the 4 cases of hernia through the foramen of Morgagni in this series, the lesion extended into the right side of the chest, although in 3 it also extended beneath the sternum. These patients presented complete hernial sacs and the round and falciform ligaments were involved in the peritoneal sacs.

Jenkinson and Roberts[3] in a series of 100 cases found the following distribution:

| | Cases |
|---|---|
| 1. Congenital | |
| Hiatus | 78 |
| Right side | 2 |
| Left side | 5 |
| 2. Traumatic | 1 |
| 3. Eventration | 4 |
| 4. Short esophagus | 5 |
| 5. Absence of diaphragm | 4 |
| 6. Thoracic stomach | 1 |

These lesions have been found at all periods of life from a few days after birth to well into old age. There is no particular sex incidence. The contents of the hernia

usually comprise omentum and transverse colon; less frequently the ascending colon, cecum, appendix, and terminal ileum are also in the hernia.

The symptomatology varies very widely. In many there are no complaints referable to the lesion and the hernia is found during routine roentgen studies or at autopsy. In others, there may be symptoms of varying degrees of severity which may simulate ulcer or gallbladder disease, or be bizarre and atypical. Severe constipation is often noted. Strangulation and obstruction, intermittent or recurrent, are relatively common and are reported in 10 to 15 per cent of the patients. Chest complaints include cough, dyspnea, and precordial pain. Frequently the symptoms are referred entirely to the chest, and there is mechanical interference with breathing and lung expansion. The discovery of the large mass in the chest is thus very apt to result in an erroneous diagnosis of neoplasm of the lung.

On physical examination, there is usually dullness over the anteromedial portion of the right lower chest, occasionally extending into the right axilla. Tympany may be present instead of dullness, however, if the herniated bowel loops are distended with gas. A succussion sound synchronous with the heart beat may occur. Borborygmi may rarely be heard. The heart may be displaced to the left.

On roentgen study of the chest, there is density over the lower portion of the right lung field in the region adjacent to the heart border and extending laterally a variable distance, in some instances entirely across the chest to the axillary border. This density may be uniform if the hernia contains only omentum or gut which is filled with fluid. In this case, there is obscuration of the outlines of the right diaphragm, lower ribs, and heart border. The density is usually rounded and presents sharply defined borders. If the colon loops contain gas, there is increased radiability over portions of the mass and colonic haustration may be demonstrable, which is pathognomonic of this condition and permits of a definite diagnosis of parasternal diaphragmatic hernia. In the lateral projection, the mass occupies the anterior and mid-portions of the right lower lung field and presents rounded, smooth superior and posterior margins; the anterior border merges with the shadow of the anterior chest wall. In every case with this type of shadow, the possibility of parasternal hernia must be definitely considered in the differential diagnosis and should be made as a tentative diagnosis until proved otherwise. The mass does not pulsate and cannot be separated from the right border of the heart shadow. Fluid levels present within the colonic loops may closely simulate encapsulated pleural fluid or abscess. Atelectasis of the right middle lobe was present in the case reported by Colmers.[4]

Barium meal and opaque enema studies are of the utmost importance in the demonstration of this lesion and should be used in all suspected cases. If the omentum only is present in the hernia, there may be only varying degrees of upward and medialward displacement of the right colon, hepatic flexure, and transverse colon. In cases with actual herniation of the colon, there is a large loop of transverse colon lying above the diaphragm with displacement of the adjacent portions of the colon toward the midline and the upper abdomen. The site of the hernia is usually at or slightly to one side of the midline. There may be separation of the afferent and efferent loops. Narrowing of the colon at the point of passage through the opening in the diaphragm is frequently seen. The stomach and jejunum are not involved in the hernia and are in normal position. Roentgenograms in the lateral projection show that the herniated loops lie well anteriorly in the chest just behind the sternum and costochondral region and are narrowed, particularly at the points of passage through the diaphragm, as noted above.

Treatment is conservative and expectant in most instances. The condition may exist for many years with no complaints refer-

able to the hernia and no apparent progression of the lesion. If incarceration or strangulation takes place, surgery is indicated unless relief is promptly obtained by enemata and other conservative measures. Surgery has been resorted to successfully in numerous instances.

## CONCLUSIONS

Parasternal diaphragmatic hernia is a relatively rare lesion but is of unusual interest to the roentgenologist as he is usually the only one capable of demonstrating the condition prior to operation or autopsy.

The hernia can frequently be diagnosed by anteroposterior and lateral roentgenograms of the chest. The presence of gas-filled loops of colon above the diaphragm in the right lower lung field is pathognomonic. The occurrence of a rounded mass in the anterior portion of the right lung field inferiorly and adjacent to the heart border requires that parasternal hernia be considered the diagnosis until it is proved otherwise.

The transverse colon and omentum are usually found in the hernia, although other portions of the intestines may also be present. There is narrowing of the loops of colon at the points where they pass through the diaphragm.

Barium enema studies are more satisfactory than the opaque meal examination in the demonstration of the lesion.

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# BILATERAL CONGENITAL FUSION OF CARPAL CAPITATE AND HAMATE

## A CASE REPORT

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BILATERAL congenital fusion of the carpal capitate and hamate appears to be a rare anomaly if judged by the number of reported cases. Kanavel's comprehensive review of anomalies of the hand published in 1932 fails to mention a single instance of such a lesion and there is no record of any similar case in recent years.

Primitive digitate vertebrates possess a distal row of five carpal bones which is reduced to four as the mammal level is reached, e.g., the rabbit, the fourth and fifth primary elements (ulnar) fusing to one carpus which articulates with the base of both fourth and fifth metacarpals. A similar state exists in some reptiles and amphibians.

According to F. W. Jones, the human carpal bones are in an extremely primitive condition from a phylogenetic standpoint. It is interesting to speculate as to whether fusion of the carpal capitate and hamate represent a phylogenetic advance. Jones quotes Bardeleben and Weidersheim as believing that seven represent the ancestral number of primitive digits and that penta-

FIG. 1 and 2. Ewing's tumor of the upper right tibia. Metastases were found in the pelvis and chest.

Fig. 3. Centers of ossification for capitate and hamate approximately normal size for age level despite fusion. Ossification of carpus reveals normal maturity except for accessory center in right scaphoid.

dactylism represents a reduction rather than a subdivision of one primary digit. Any reduction in the number of carpal bones under this theory would thereby be considered a phylogenetic refinement.

## CASE REPORT

L. R., white male, aged nine, entered Children's Hospital, Service of Dr. Paul W. Sutton, on March 21, 1942, because of a painful tumor over the right upper tibia. He first complained of pain just below the knee in September, 1941, at which time he had a low grade fever. He suffered with recurrent attacks of pain and fever until January, 1942, when swelling over the leg was observed. The pain and swelling had increased to such an extent as to prevent walking during the exacerbation. There was no weight loss and the remainder of the history was noncontributory, except that the child was obviously feeble minded. Kahn and Wassermann tests were negative. Roentgenograms (Fig. 1 and 2) suggested Ewing's tumor or osteomyelitis, more likely the former, so that roentgen examination of the entire skeleton was carried out at which time the anomalies of the carpal bones of both wrists were noted (Fig. 3). Biopsy of the tibia was done on March 27, 1942. The sections were examined by Dr. James Ewing who made a diagnosis of endothelioma. After an extensive course of roentgen therapy and in the absence of evidence of metastases, a mid thigh amputation was done on June 13, 1942. Another roentgen examination in October, 1942, revealed multiple chest metastases.

Roentgenograms of the wrists of both mother and father were normal.

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# A VERTEBRAL ANOMALY: PROBABLE PERSISTENT NEUROCENTRAL SYNCHONDROSIS

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RECENTLY I had the opportunity of examining 2 patients who presented an identical spinal anomaly, and because a careful search of the literature failed to reveal any illustration or definite description of this condition, it was regarded as worthy of being recorded. In both instances the findings were incidental and had produced no symptoms.

Case I. G. V., a white girl, aged twelve, had had epilepsy following a post-measles encephalitis at the age of seven. There were no symptoms referable to the spine or spinal nerve distribution. There was no history of injury to the spine.

Fig. 1. Case I.

Figure 1 is an anteroposterior view of the upper dorsal spine. It shows a slight broadening of the third dorsal vertebra with a narrowing of the intervertebral space between the third and fourth dorsal vertebrae. When, however, the tube is angled 10 degrees toward the feet, as in Figure 2, there is seen a diagonal radiolucent line traversing the upper right margin of the third dorsal vertebra. The projection creates an illusion of seeming fusion of the bodies of the third and fourth dorsal vertebrae. The spinous process of the third dorsal vertebra is hypoplastic, but there is no spina bifida. An anteroposterior view of the cervical spine also showed this defect in the third dorsal vertebra, as might be expected, since the rays reaching this vertebra would be caudad. Figure 3 is a lateral view of the upper dorsal region. It shows the narrowing of the intervertebral disc between the third and fourth dorsal vertebrae.

Case II. V. S., female, white, aged twenty-one, was in an automobile accident shortly before being examined, She gave no previous his-

Fig. 2. Case I.

tory of injury. She had considerable pain, and the roentgen examination showed an anterior wedging of the third dorsal vertebra, plus a fracture of the superior surfaces of the fourth and fifth dorsal vertebrae and a fracture of the left transverse process of the fifth dorsal. In addition, there were marked hypertrophic spurs between the third and fourth dorsal vertebrae

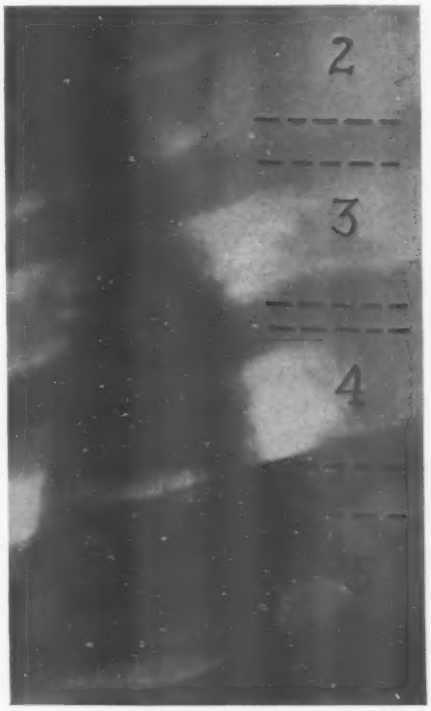


Fig. 3. Case I.

and a sharply localized kyphos in this region, shown in Figure 4.

In this case, an anteroposterior view of the upper dorsal region (Fig. 5), shows the same type of radiolucent line separating the left upper lateral corner of the body of the second dorsal vertebra. It is visualized in the anteroposterior view without angling of the central ray because the vertebra is angulated forward by the kyphos just below it. Note that in each instance the separated corner of the body of the vertebra is slightly elevated, producing a slight tilting of the superior surface of the vertebra and a consequent slight localized scoliosis. In this case, also, there is a false appearance of fusion of the involved vertebra and the one next below, owing to the non-perpendicular angle of incidence of the rays plus the actually narrowed

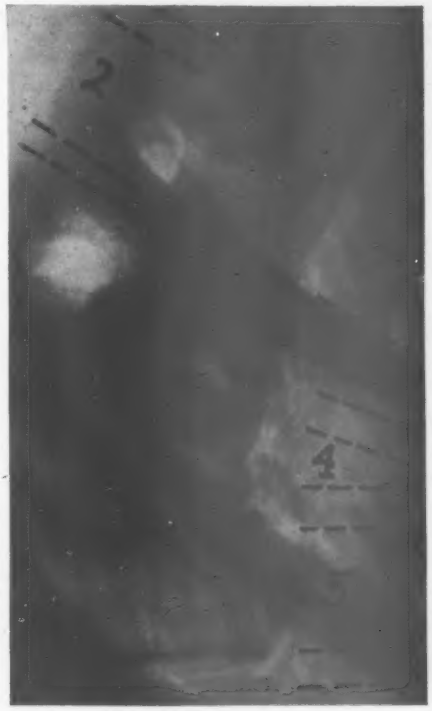


Fig. 4. Case II.

Fig. 5. Case II.

intervertebral disc space that is present here. In oblique views of the upper dorsal spine, the defect in question could not be visualized. A planigraphic study shows that the defect, slightly curved with convexity downward and inward, lies posteriorly in the body.

In the cases that have been presented, the defect is located on the left side in one case and on the right side in the other, and the appearance of one is almost a mirror image of the other. In both cases the involved upper lateral angle of the vertebral body has become somewhat overdeveloped and more prominent than normal, causing a slight tilting of the superior surface of the body of the vertebra. In both instances, the affected vertebra was associated with some abnormality of the intervertebral disc just beneath it, consisting chiefly of narrowing, and in both cases the spinous process of the involved vertebra was hypoplastic. In both, the upper dorsal region of the spine was involved. And, in both cases, in order for the defect to be visualized, the incident beam had to traverse the vertebral body in a somewhat caudal direction with respect to its sagittal axis.

The interpretation of the appearance described in these 2 cases lies between an acquired defect such as a fracture and a developmental anomaly. The chief evidence for this being a fracture is that the defect does not correspond exactly with any recognized developmental structure. The evidence against this being a fracture is as follows: (1) Whenever a rigid arch is broken, two sites of fracture must ordinarily occur. (2) The appearance is not that of a fracture. The margins of the defect show a narrow uniform zone of increased density, a bony cortex, such as occurs in a persistent ununited epiphysis. (3) Both cases showed no change after a considerable interval of time (fourteen months in Case I and five months in Case II). If this were a fracture, then with the rigid fixation that the mechanics of the arch would provide, one would certainly expect union to occur. Even if one postulates non-union in such a fracture, changes such as increased perifocal sclerosis, external callus, hypertrophic exostoses, etc., should occur, and absolutely no change occurred in the time intervals noted. (4) There is no history of trauma in either case (in Case II the known injury could not have produced a fracture that looked old immediately following that trauma). (5) The involved angle of the vertebral body is overdeveloped. There should have been no change if the defect were a fracture. (6) The symmetrical placement and appearance in the 2 cases favors a developmental defect rather than a fracture. (7) While the associated narrowing of the subjacent intervertebral disc could be traumatic, the associated hypoplastic (or absent) spinous process in each case favors the lesion being developmental.

In order to discuss the defect from the standpoint of a developmental anomaly, a brief consideration of the ossification of the vertebra will be helpful. The vertebra is derived from six primary cartilaginous centers. There are two paracentral centers for the body, one for each half of the neural arch and one for each costal process. Ossification takes place in a corresponding manner, although the two lateral centers of the body fuse early and so quickly that it is generally stated that the body arises from one center of ossification. Transitory cephalad and caudad centers may also be present at the beginning, but these also rapidly fuse ordinarily. Recently Ehrenhaft has presented evidence of an anterior and a posterior center of ossification in the body, which also quickly fuse. It is thus seen that there is a multicentric origin of ossification of the vertebral body, following a certain pattern, but ordinarily these multiple centers rapidly fuse to form a single center. Failure of fusion of certain of these centers or their failure of development results in some well known vertebral anomalies, such as anterior spina bifida and hemivertebra. The ossified lateral halves of the neural arch generally fuse by the end of the first year of life. The neural arch fuses with the body of the vertebra between the ages of three and six years. However, the ossifica-

tion center (or centers) of the body does not give rise to the whole of the body, since the posterior lateral portions of it (about one-sixth) are ossified by extensions of the neural arch ossification centers. The cartilage zone that is interposed between the ossification center of the body and that of the neural arch extension on each side is known as the neurocentral synchondrosis.

This synchondrosis runs vertically through practically the entire height of the vertebral body, even though the pedicle of the vertebra arises from the superior portion of the posterolateral aspect of the body. As a result, roentgenograms taken of the dorsal spine of two and three year old boys, directing the central ray from 10 to 25 degrees caudad did not reveal any defect resembling that described above, and this lack of visualization is what one would expect, since the synchondrosis runs vertically and would not be in the plane of the central rays.

The evidence for this defect being a developmental anomaly has already been presented above in the arguments against its being a fracture. The fact that it runs diagonally caudad through the superior posterolateral aspect of the vertebral body instead of vertically through it is the chief objection against concluding that it represents a persistent ununited neurocentral synchondrosis. In order to consider it as such an anomaly, one must postulate that the disturbance that prevents fusion also causes an oblique placement of the synchondrosis. This is not improbable, and until a specimen of such a vertebra is available for pathological study, an interpretation of the defect being reported here as a persistent ununited neurocentral synchondrosis seems to be a justifiable working hypothesis.

SUMMARY

Two cases of a hitherto unreported vertebral anomaly, probably a persistent neurocentral synchondrosis with some associated slight changes, are presented, with a discussion of the condition.

The author wishes to express his thanks to Dr. O. V. Batson, Professor of Anatomy in the Graduate School of Medicine of the University of Pennsylvania, for his helpful suggestions.

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# TRACHEOCELE*

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DIVERTICULA of the trachea are infrequent coincidental findings at necropsy and are rarely diagnosed clinically. The limited number of cases reported in the literature have been described under various descriptive titles such as aerocele, bronchocele, tracheaectasy, tracheal hernia, and tracheaectasis.

The "aerial goitre" was familiar to observers as early as the fifth century. Most of our knowledge of this abnormality of the trachea was known prior to the present century. This is interesting when one recalls that much of the progress in the diagnosis of diseases and anomalies of this portion of the respiratory tract has been made in the past twenty years.

The case which is reported below is an excellent example of the truth of the old adage that "all that wheezes is not asthma." This patient was hospitalized because of choking spells, dypsnea, and wheezing with a clinical diagnosis of asthma.

## CASE REPORT

A white male, aged thirty-two, was admitted to the hospital on July 1, 1943, complaining of choking, coughing and shortness of breath.

For the past eight or nine years this patient had had repeated episodes of coughing, wheezing, and shortness of breath, all of which occurred in the fall and winter months.

In the summer of 1942, he developed an upper respiratory infection associated with blood-streaked sputum. He was actually ill for only a few days. Following this illness, he felt well until December, 1942, when his symptoms of coughing, choking sensation and shortness of breath became more constant.

He never noticed chills, fever, chest pain, or expectoration of any type. On occasions, he would be awakened in the night because of coughing and shortness of breath.

His family history was of no clinical significance. He had an appendectomy in 1938; other than this there had been no illness requiring medical attention.

Physical findings on admission to the hospital showed the patient to be well developed and fairly well nourished. He was short of breath on moderate exertion. There was no cyanosis. No masses could be palpated in the neck. The thorax appeared to be disproportionately large in the anteroposterior diameter as compared with the transverse diameter, and displayed a diminished visible expansion on inspiration. There were rhonchi heard both on inspiration and expiration diffusely disseminated throughout both lung fields. The heart showed no abnormalities. The blood pressure was 120/80, the pulse was regular. The remainder of the examination was normal.

Laboratory findings were essentially normal. Numerous sputum examinations were negative. The patient was tested by the scratch method with many of the more common allergens, and no significant reactions were noted.

Roentgen examination of the chest revealed a slight increase in radiability of both lung fields and low flattened diaphragms consistent with the diagnosis of moderate emphysema. A bronchogram (Fig. 1) showed a cylindrical bronchiectasis of the medial basilar bronchi of both lower lobes. There was also a saccular type of dilatation of the upper third of the trachea (Fig. 2) beginning approximately 4 cm. distal to the larynx. The air-filled diverticulum measured 5 by 4 by 5 cm. in size and originated from a wide neck at the posterior right lateral portion of the trachea. This saccular dilatation displaced the barium-filled esophagus (Fig. 3) to the left and posteriorly. There was also moderate narrowing of the lumen of the esophagus in this area: this, however, was not sufficient to obstruct the flow of thick barium mixture. The lumen of the entire trachea distal to the diverticulum was 5 to 8 mm. wider than normal. There was definitely some redundancy of the trachea, more obvious just distal to the tracheocele.

Bronchoscopic examination revealed approximately the above findings. The entire sac appeared to be covered with normal tracheal

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epithelium, and there was no evidence of retained secretion in the diverticulum. The opening of the saccular dilatation into the lumen of the trachea was almost as large as the sac itself.

While in the hospital, his course was uneventful, and his symptoms were fairly well controlled with bed rest and sedatives.

COMMENT

Chiari[1] carefully studied both grossly and microscopically 5 cases presenting

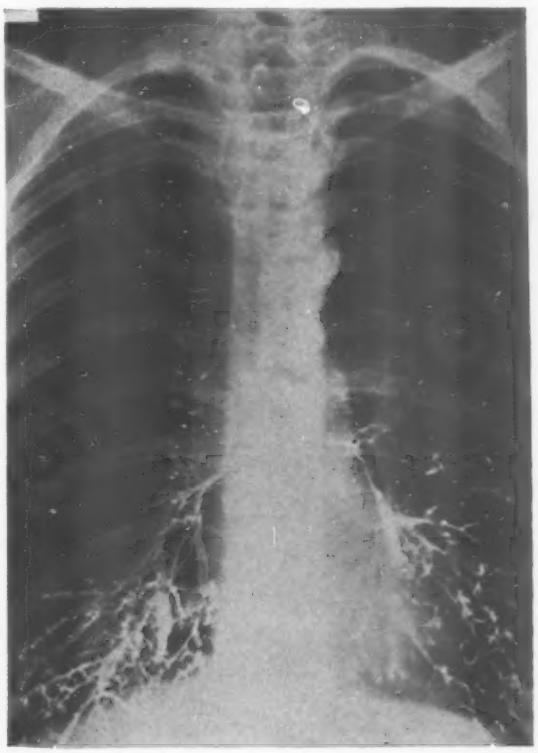

Fig. 1. Posteroanterior bronchogram showing the cylindrical bronchiectasis of the medial basilar bronchi of both lower lobes.

small diverticula of the trachea at necropsy. These all occurred on the right side of the trachea between the seventeenth and twenty-second tracheal rings and the largest measured 6 mm. in width and 12 mm. in length. He was inclined to believe that all of these cases were congenital in origin, and that diverticula of this type were found at the sites where supernumerary bronchi were prone to occur. However, he

Fig. 2. Left anterior oblique view demonstrates the tracheocele (arrow).

Fig. 3. Air-filled tracheocele anterior to the barium-filled esophagus.

was reluctant to exclude the possibility that diverticula of the trachea could occur by the combination of infection in the mucous glands and increased intrabronchial pressure produced by a chronic cough. Choruzenko's[2] case illustrated this possibility.

Miller,[4] in his excellent histologic study of the trachea, describes the posterior wall of the trachea as composed of isolated bundles of trachealis muscle bridging the cornu of the semi-rings of the trachea. Between bands of muscle lie relatively amuscular areas. Development of small diverticula in these amuscular areas seems quite feasible, especially should there be infection of the mucous membrane and chronic cough with resulting episodes of markedly increased intrabronchial pressure. Kahlstrom[3] reported a case where the patient had a chronic cough and physical and roentgenographic evidence of chronic pulmonary infection. At necropsy a series of diverticula were found along the posterior portion of the trachea and larger bronchi in the intercartilaginous amuscular areas, the largest of which measured 7 mm. in depth.

Stibbe[6] states that the congenital type have narrow mouths, and the acquired type a wide mouthed orifice. According to his criteria, the case we have reported would be of the acquired type, and this might seem to be borne out by other evidence of infection of the tracheobronchial tree. However, one cannot forego the thought that were not the infection preceded by an inherent weakness of the posterior tracheal musculature, this tracheocele might never have developed. It is also interesting to speculate as to whether or not the enlargement of the entire trachea was congenital or acquired and also what part, if any, this played in the production of the large diverticulum.

Olmer, *et al.*[5] described a diffuse dilatation of the trachea in a case that is very similar to ours. Their patient, however, had no tracheal diverticulum or bronchial lesion.

With the more common use of the bronchoscope and bronchography, other lesions of this type will be found and studied.

## SUMMARY

A case of tracheocele is presented and its probable pathogenesis is discussed. This case was considered to be primarily a congenital defect in the posterior tracheal musculature, with production of a diverticulum by increased bronchial pressure produced by coughing.

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# RADIOTHERAPY IN DUPLAY'S DISEASE

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THE roentgen examination of the shoulder reveals, not uncommonly, the presence of calcium salts in the periarticular soft tissues, frequently between the acromium and the head of the humerus.

These shadows were first described by Painter in 1907. Other investigators (Bergman, Stieda, and others) described them as simple calcareous deposits in the soft tissues.

According to various authors the calcification results from "bursitis" (Codman, Buchner, and others), whence the name of "bursitis deltoidea" or "bursitis calcarea."

Others regard the disease as being a calcified periostitis (Painter, Haenisch, Dickson, Crosby).

Mayer, as well as many others, has identified this morbid condition with that described by Duplay in 1870 under the name of "scapulohumeral periarthritis."

Similar shadows were observed in different articulations other than those of the shoulder by Schmidt, Stegemann, and others.

In 1929, Sandström described his observation at the Hospital Maria in Stockholm, to show that the calcareous shadows are found in other articulations, but less frequently than in the shoulder.

In all the articular localizations there are perfectly analogous local symptoms. According to his opinion the condition is a clinical entity for which he proposed the designation of "peritendinitis calcarea."

Some details about the localization of the calcareous deposits are still controversial. The majority of authors are of the opinion that calcification takes place in tendons and tendinous tissues, and that the bursa is secondarily involved by inflammatory reaction, generally remaining free from calcareous accumulation.

According to Carnett's opinion, the lesion begins with a tendinitis which ends in local necrosis and posterior calcification.

## ETIOLOGY

Regarding the etiology of Duplay's disease, authors differ in their opinions; many causes have been considered but no agreement has yet been reached.

For a long time it was believed that traumatism was an important causative factor, but actual observations do not confirm this point of view, the traumatism being merely regarded, in some cases of the disease, as a simple incidental agent.

It is of interest to draw attention to the similarity existing between this disease and that of Pellegrini-Stieda, i.e., post-traumatic para-articular ossification of the knee joint.

Unaccustomed and exaggerated exercise has also been pointed out as a cause. We have even seen cases in which a simple quick movement has caused the appearance of the typical symptomatology.

Codman asserts that either strain or traumatism may produce little dilacerations in the tendon of the supraspinatus causing clots of blood in the spot where chalky formations will be found later.

Besides the agents mentioned, focal or bursal infections, endocrine disorders, especially those of the parathyroid and even certain metabolic disturbances have been pointed out as causes of predisposing agents of Duplay's disease.

## SYMPTOMATOLOGY

In view of its evolution, Duplay's disease may be divided, in an arbitrary way, into several periods, designated by Codman: (*a*) acute or spastic; (*b*) subacute or adherent, (*c*) chronic; (*d*) latent.

According to Lattman no exact limit exists between these periods.

If, after an acute attack, a new crisis with the same symptoms on the same side occurs within a short time (from two to four weeks), this relapse may be considered as being the subacute period. According to

Codman's opinion it is during this period that adhesions in the bursa are formed.

The acute form presents the following symptoms:

*Pain.* After trauma, or even without any apparent cause, a very sharp pain radiating down the arm and up to the cervical region suddenly manifests itself. The acute pain is felt in the greater tuberosity of the humerus. The spontaneous pain is sometimes so severe that it causes nausea, and pressure is so intolerable that the contact of clothing becomes unbearable. The radiation of the pain may even extend to the extremity of the fingers. The exact diagnosis for such a sudden pain, when there is no record of trauma, and with this radiation suggesting the distribution of the brachial plexus, is by no means easy, sometimes leading to the diagnosis of a plexitis. The pain often extends to the thorax, in certain conditions causing precordial pain.

We have had the opportunity of observing a patient whose pain suddenly manifested itself during the night, radiating with such intensity down to the arm and to the precordial region that he declared he felt the sensation of approaching death, this complete symptomatology simulating an acute crisis of heart disease. In such cases the diagnosis of cardiac infarction or angina pectoris is not infrequently made.

*Restriction of Mobility.* The pain is followed by an acute spasm of the shoulder muscles with consequent diminution of mobility. This limitation of movement is of various degrees, those of outward rotation and abduction being most acutely affected.

In severe cases, both active and passive movements are limited or even impossible, but in mild cases passive mobility can be maintained to a great extent.

*Calcification.* Calcification is shown roentgenologically. The chalky deposits can attain considerable size. It may be observed that the roentgen examination shows only faint calcareous shadows.

There are clinical cases presenting subjective symptomatology, in all ways similar to that of Duplay's disease, in which the calcification does not appear in the roentgenogram. Some of these cases are incipient forms of Duplay's disease in which calcification is not yet sufficient for roentgen visualization. However, in cases in which clinical symptoms persist for a long time, without the roentgenological detection of chalky deposits, the diagnosis of Duplay's disease cannot be confirmed.

The size and number of the calcareous deposits are not necessarily proportional to the intensity of the symptoms.

Unilateral pain in patients suffering from bilateral calcification is a frequent occurrence. This fact, as well as the presence of the typical pain in the absence of calcification, makes the relation between the pain and chalky deposits difficult to interpret.

Besides the symptoms which have been mentioned, there are others which may appear during the acute period; for instance, external signs of inflammation such as redness, heat, swelling, pain, and fever. The last symptom is rare but there are cases in which the temperature rises to 40° C.

In the subacute state or even in acute crisis of the chronic period the symptoms are similar to those of the acute form, although less intense but of longer duration.

In the chronic stage, pain is present in a mild degree. The principal symptom is the limitation of movement differing from that of the acute form inasmuch as there is no muscular spasm. The arm can be abducted at most to a right angle with the body. It is in this position that the patient generally feels the greatest pain, but after passing this point he can raise his arm and rotate it backwards without acute pain.

The pain again reaches its maximum when the arm reaches the right angle in the downward movement. This is probably due to the fact that at this angle the bursa is compressed between the greater tuberosity of the humerus and the acromion.

There is a test recommended for observing the intensity of a case: the patient is asked to touch his ear on the side opposite that of the involved shoulder, passing his arm over his head.

There are latent cases with lack of subjective symptoms, in which, during the roentgen examination, chalky deposits, typical of the disease both in form and localization, are accidentally found.

In 20 cases of this kind cited by Lattman the patients were observed during a period of more than five years; 12 of them sooner or later manifested the remaining symptoms of Duplay's disease, some of them attributing the incidental cause to trauma.

### DIFFERENTIAL DIAGNOSIS

The differential diagnosis must be made from articular diseases such as tuberculosis, lues, cystic bone lesion, giant cell tumor, osteomyelitis and malignant tumors.

Acute cases can easily be confused with acute septic conditions as, for instance, arthritis, osteites and phlegmons.

Furthermore, as already stated, it is not difficult to confuse the symptoms of Duplay's disease with those of neuralgia, brachial plexitis, rheumatism and occasionally with angina pectoris.

The exact diagnosis must be made by a careful anamnesis, local and roentgen examinations.

### ROENTGENOLOGICAL DIAGNOSIS

In the majority of cases the calcification is easily visualized but it is advisable to make two exposures, one with external and one with internal rotation of the humerus.

As bilateral affection is of frequent occurrence, even when the symptoms are unilateral, it is advisable to roentgenograph both shoulders.

As already stated, the calcareous deposits may be either simple or multiple.

The most frequent localization is near the greater tuberosity of the humerus; sometimes, however, the deposit is found below and in front of the glenoid cavity in the acromion, in the coracoid apophysis or in the vicinity of the lesser tuberosity of the humerus.

Due to the intimate proximity of the anatomical structures of the shoulder it is impossible, in a great number of cases, to determine the strict anatomical localizations of these deposits.

The most important thing in the differential roentgen diagnosis is the observance of fracture of the greater tuberosity of the humerus, which can easily simulate a subacromial calcified bursitis, especially when the fractured tubercle is drawn by the inserting tendon of the supraspinatus. However, the fracture is always detected on the roentgenogram.

### TREATMENT

Many forms of treatment have been applied with more or less success.

A simple immobilization of the arm by means of splints and the use of analgesics, even opiates, according to the case, are sometimes tried in the acute phase, and in a great number of cases improvement is observed within six to eight weeks.

Other cases develop into subacute or chronic forms and symptoms can subside or recur frequently.

One case is cited in which a patient who refused any kind of treatment had frequent relapses during a period of twelve years.

Some surgeons and orthopedists, even in cases in which calcareous deposits are found, recommend clinical therapy, reserving surgical intervention only for cases in which a fair trial has been given to all other kinds of treatment, but without results, and when the symptoms, especially pain and limitation of movement, persist.

Physiotherapy has been widely used in various forms including heat, diathermy, sinusoidal and galvanic current, ionization and all forms of massage as well as active and passive movement.

According to Sandström, massage is contraindicated, because he declares it aggravates the symptoms.

At present radiotherapy is being more and more indicated as the most effective therapy in Duplay's disease.

If we consider bursitis as an infection, the beneficial effect of radiotherapy may be explained by the property of roentgen rays to destroy innumerable cells in the

seat of infection, liberating antibodies and lysins which destroy the focal infection.

According to Heidenhain and Fried, its action may be explained by the regressive effects upon the infiltrates in consequence of the liberation of leukocytes.

If we consider the principal symptom in Duplay's disease as a neuralgic manifestation or simple neuritis of the coracoacromial process we can explain the action of the roentgen rays in two ways: (1) According to Freund, Holfelder, Weinberg and various other authors, the beneficial action brought about by radiotherapy is caused by the ability of the rays to relieve congestion and so bring about relief of the compression of the perineural tissues. (2) In Strauss's opinion, variation of the cholesterin-lecithin reserve caused by the treatment is of great importance in the mechanism of nervous action.

Here we must take into consideration the similarity existing between calcified bursitis and post-traumatic osteoma.

Olivier considers the osteoma as a development of periostitic fragments in the muscles, but we can regard it as a simple precipitation of calcium related to a local physicochemical modification, the calcium coming from adjoining bones by way of the humoral or fixing itself directly upon the coagulated blood.

A mechanical factor, be it sudden, prolonged or repeated, is capable of bringing on these benign tumors.

According to Chauvet, Didiée and Pasteur, the earlier the radiation treatment of osteoma is undertaken, the more efficacious it will be and it should consist of intensive local doses repeated daily.

With the suppression of pain, an early result of radiotherapy, normal mobility is restored and the patient can return to his usual activity sooner than from any other treatment.

During the first twenty-four hours after the irradiation, the symptoms are sometimes aggravated, but the following twenty-four hours bring a great relief in the pain and limitation of movement.

In the acute cases, evolution after the treatment is generally as follows: (*a*) speedy or slow amelioration of subjective symptoms, always with simultaneous improvement of the objective symptoms; (*b*) the remaining less intense symptoms gradually disappear, with total reabsorption or at least decrease of the chalky deposits. The latter fact deserves special mention.

With repeated roentgenograms Sandström followed, minutely, the disappearance of the process. In some cases the deposits disappeared in two or three weeks but sometimes more slowly. The patient, however, became symptom free even when the chalky deposits were still present, though reduced in density or size.

There are references in the literature to cases in which complete disappearance of the concretions was not noticed, these forms generally presenting bony structure due to secondary osteoblastic formation.

Acute symptoms which usually persist for one or two weeks, in the irradiated patients continue no longer than from three to five days.

Recently Weinberg in his 161 observations declares having frequently obtained extraordinary results which surprised not only the patients but also himself.

In only 5 cases, i.e., in 3.1 per cent, were favorable results not obtained.

## TECHNIQUE OF TREATMENT

From the standpoint of treatment the existence of a calcareous formation must be considered even though admitting its inflammatory etiology.

We use an average dosage of 150 to 200 r, and six or more applications, with an interval of two or three days between treatments. The low dosage that we use, principally in the first application, is justified on account of the inflammatory process, but the repetition of these doses is necessary in order to obtain the disappearance of the calcification.

With this technique, while avoiding too intense primary reactions, we take care of

all the clinical manifestations of Duplay's disease.

## REPORT OF CASES

We have treated 30 cases by radiotherapy, but only 18 with sufficient post-therapeutic observation. Of these 18 cases 15 became symptom free, or 85 per cent favorable results. Of these 15 cases, 6 were re-examined roentgenologically, disappearance of the calcification being observed in all of them.

In the other 3 cases, we obtained only symptomatic amelioration. In 1 of these, roentgen examination could not be made after treatment, the second case showed a good temporary result but later recurred, and the third was our only case in which no improvement was observed.

We will present some cases showing interesting findings.

FIG. 1. Case 1. Roentgenogram of the shoulder before treatment.

FIG. 2. Case 1. Roentgenogram of the shoulder after treatment.

CASE 1. C., J. S., male, aged thirty-six.

*Complaint.* Violent fall twenty days before consultation. Severe pain set in four days ago in the left shoulder with scapulohumeral articulation.

Roentgen examination showed "calcification of the subacromial bursa." Even with only unilateral manifestation roentgen examination of the other shoulder demonstrated a bilateral Duplay's disease. This case corresponds, so we believe, to a latent form according to Lattman's classification.

*Result.* Disappearance of all the subjective symptoms. Later re-examination showed disappearance of chalky deposits after radiotherapy.

CASE II. C., F., male, aged fifty-eight. For two and a half months, stitch-like pains in the left shoulder and complete limitation of movements occurred without apparent cause. Special references were made to precordial radiation of the pain leading to the supposition of heart disease. Roentgen examination revealed a calcification of the subdeltoid bursa. Two series of 6 roentgen treatments were given.

*Result.* After the first series of treatments both the pain and mobility have greatly improved, abduction showing less amelioration than other movements. After the second series there was complete disappearance of all symptoms. The roentgenograms no longer showed any signs of Duplay's disease.

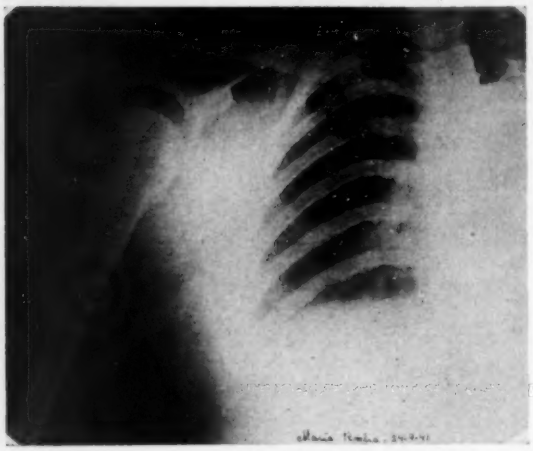

FIG. 3. M. R. Roentgenogram upon which the diagnosis of Duplay's disease was based.

CASE III. C., C., male, aged forty-three. For the last week the patient had suffered from severe pain in the right shoulder with complete limitation of movement. Redness and swelling. A three year old roentgenogram showed calcification of the subdeltoid bursa although symptomatology was lacking. A new roentgenogram confirmed the existence of Duplay's disease.

*Result.* A short time after roentgen treatment the patient was able to play tennis again. Roentgenogram reveals no signs whatever of the disease.

CASE IV. S., E. T., male, aged thirty-six.

*Complaint.* For four years diffuse pain in the left shoulder. Six or seven days after a violent movement, a severe crisis in this shoulder occurred with complete limitation of movement. A roentgenogram revealed a calcification of the subdeltoid bursa.

*Result.* Complete disappearance of the symptoms and roentgen signs.

To avoid useless repetition we shall cite no other cases.

FIG. 4. M. R. Roentgenogram taken after treatment in which the bony aspect changes the clinical opinion as to the previous state of the patient.

## DIAGNOSTIC PROBLEMS

Some fundamental details of the diagnosis seem to call for special mention; first, the frequency of the diagnosis of brachial plexitis in cases in which a roentgen examination reveals a calcification of the subdeltoid bursa; second, the fact that in some clinically diagnosed cases of Duplay's disease the most careful roentgen study is unable to detect the presence of a chalky deposit.

In our experience, in only one of the cases in which we failed to get results, could the roentgenological verification of Duplay's disease never be obtained. The same patient underwent other treatments for several months without results.

Our particular case showing the difficulty of the differential diagnosis, even with all positive clinical tests, deserves to be mentioned.

M. R., female, aged thirty-nine. More than twenty years ago, she suffered for the first time from a pain in the right scapulohumeral articulation resulting from a strain of the arm. Since then any forced elevation brings on the same painful impression of luxation. Four months ago, intense pains were felt with remissions, until eleven days ago, when the pain became most severe and permanent, preventing any movement of the articulation which was also sensitive to touch, with swelling and redness of the whole region. Edema of the whole arm. Fever. The roentgenogram revealed calcification of the subdeltoid bursa.

*Result.* Immediately after the first treatment the pain diminished in intensity and at the end of the treatment movements were free, although slight pain persisted during movements of rotation and abduction. At present, she feels pain in the right shoulder which has no relation, however, to movements.

A roentgenogram shows complete disappearance of the calcification but inside the trochiter invading the articular surface, there is a process of bone destruction with the formation of an irregularly limited concavity. The roentgen image of the referred process is common to luetic osteomyelitis, or tuberculous gumma.

This case has not yet been completely understood by the orthopedists who are still studying it.

The latest roentgenogram excludes this case from the failure of roentgen therapy.

We have decided to present this case considering the possibility of uncommon complications of diagnosis. As is to be seen, all the circumstances—subjective symptoms, objective symptoms and even roentgen examination—led to the diagnosis of Duplay's disease, which, later on, had to be rejected.

## CONCLUSIONS

1. The roentgenological confirmation of the existence of chalky deposit is a necessary proof of Duplay's disease.

2. Roentgen treatment must be carried out with moderate doses, because of the inflammatory process, and by repeated applications in order to obtain the disappearance of the calcification.

3. According to our observations the good results obtained by means of radiotherapy are fully confirmed in well identified cases of Duplay's disease.

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# A RAPID RADIUM IMPLANTATION METHOD FOR RODENT ULCER

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IN A previous communication,[1] radium implantation for rodent ulcer (basal cell carcinoma) in the vicinity of the eye was described, and the general conduct of such cases discussed. Seventy-six patients treated in the years 1930 to 1935 were dealt with; only 2 failures occurred, and the incidence of eye damage was very slight except in the case of lesions involving the upper lid. This latter circumstance was explained on physical grounds. The method was regarded as particularly suitable for the most awkwardly placed of these neoplasms near the eye.

Passage of time has not altered the conclusions arrived at, but a modified method has been evolved which has the advantages of compressing treatment into thirty hours, and of giving better cosmetic results. There has been no damage to the eye, even in the case of the upper lid lesions where the risk is greatest. Further, the great flexibility of the method as regards both area and difficult contours is of peculiar value in this type of case since a flat field is rarely obtained, especially at the common inner canthus site. The efficiency of the method and the lack of conspicuous tissue change render it well worth the short time involved; patients can have the treatment one forenoon and go home the next afternoon, being in the hospital for one night only, unless they wish to stay longer.

The method was put into use in May, 1939, and is therefore of comparatively recent development, but with this type of tumor it would appear reasonable to draw some deductions. At the time of writing the earliest cases are of over four years' duration.

## THE METHOD

Details of the implantation method were given in the original paper, and it will therefore suffice to state that the operation is carried out after minimal injection of 2 per cent novocain with adrenalin and that painting the skin with proflavine oleate 1 per cent in liquid paraffin[2] deals with any local sepsis. The needles used (Fig. 1) are of small dimensions having a total length of

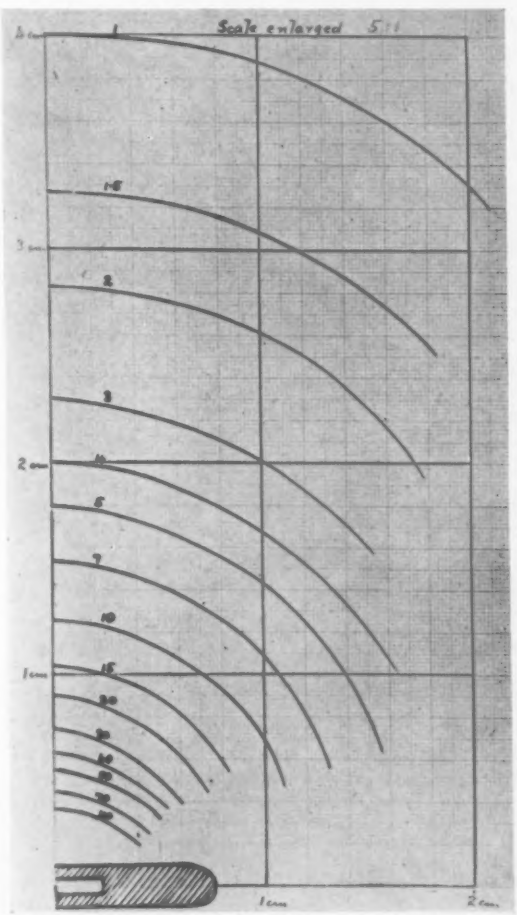


FIG. 1. Isodose curves round 2.0 mg. needle, 15 mm. long, 0.6 mm. Pt wall and active length 4.5 mm. Half the needle is illustrated; the curves are drawn as dictated by convenience and not in arithmetical progression.

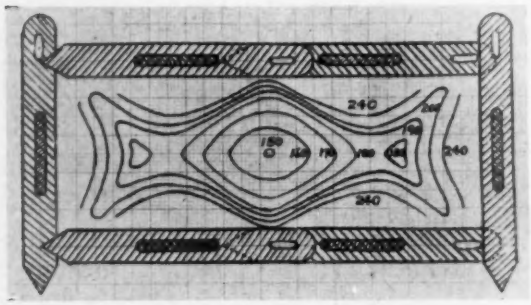


Fig. 2. Isodose curves within the basic 2.5 by 1 cm. plane (roentgens per hour).

15 mm., with an active length of about 5 mm., 0.6 mm. platinum walls, and radium content 2 mg. (element). Each needle is retained in position with a fine silkworm stitch across the puncture. The shortness of the individual needle renders the plane very adaptable to the circumstances of each case.

The basic arrangement is a rectangular plane 2.5 by 1 cm. in size, made of six such needles (Fig. 2); a four needle square is hardly ever large enough. As has been said, this is readily fitted in to varying contours, and expanded as required, in which case the necessary center line will contain less radium than either side. For "filling in" the larger rectangle the most appropriate size in the Western Infirmary stock is 20 mm. long, 8 mm. active length, with 1 mg. radium (element) and 0.6 mm. platinum filtration. In a number of cases the 2 by 2.5 cm. planes have had a center line made of the 2 mg. needles, and the higher dose still seems within the limit of what can be tolerated without tissue damage. The implant is carried out as nearly as possible 0.5 cm. below the skin and the dose distribution "at the skin" is illustrated in Figure 3. Since no operator, however experienced, could

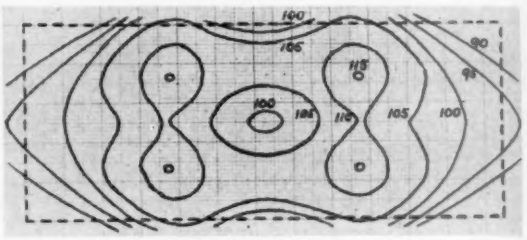


Fig. 3. Isodose curves 0.5 cm. away from 2.5 by 1 cm. plane showing uniformity of dose rate at presumed skin surface (roentgens per hour). Dose taken as 100 r/hr. × 30 hr. = 3,000 r.

Table I

SOME REPRESENTATIVE DOSAGE RATES IN RADIUM IMPLANTS
(roentgens per hour)

| | | In Plane | 0.5 cm. from Plane |
|---|---|---|---|
| Standard six needle implant. 6×2.0 mg. radium element, 15 mm. long, 2.5×1.0 cm. | Center | 150 | 99 |
| | 0.8 cm. from center on long axis of rectangle | 190 | 104 |
| Ten needle implant. 10×2.0 mg. radium element, 15 mm. long, 2.5×2.0 cm. | Center of one rectangle | 174 | 122 |
| | 0.8 cm. from center on long axis of rectangle | 216 | 145 |
| | Center of whole figure; i.e., over central line of radium | — | 131 |
| Ten needle implant. 8×2.0 mg. radium element, 15 mm. long, 2×1.0 mg. radium element, 20 mm. long. 2.5×2.0 cm. | Center of one rectangle | 148 | 104 |
| | 0.8 cm. from center on long axis of rectangle | 186 | 129 |
| | Center of whole figure | — | 105 |

claim to place the needles exactly at this depth, the skin dose will presumably vary between the rates shown "in plane" and "0.5 cm. away," but the skin effects observed indicate that something near enough to the ideal arrangement is very usually attained (Table 1). This is so even when the thickness of tissue is slight.

During treatment the eye is not bandaged over since this tends to produce conjunctivitis (Fig. 4 and 5) and acriflavine drops 1:1000 are used freely. After removal of the needles, the skin is gently washed and sterile sulfanilamide powder carefully dabbed into the punctures, and over the treated area. This keeps the skin both clean and dry, thereby reducing reaction, and a clean protective scab generally forms so that no dressing is required in many cases.

The patient is advised to avoid undue exposure for a day or two as a precautionary measure. A simple boracic eyewash is prescribed and the treated skin should be kept dry. As will be seen from Figure 3, the skin dose is approximately 3,000 r in thirty hours. The usual reaction consists of erythema and dry desquamation, and only where there has been epiphora is a moist reaction likely, unless there is a good deal of local ulceration to start with. Some transient congestion of the adjacent conjunctiva occurs. The cosmetic results are usually excellent, and the punctures prove inconspicuous as a rule, perhaps because they are open for so short a time.

FIG. 4. Implant in position for rodent ulcer at outer canthus.

FIG. 5. Method of dressing implant shown in Figure 4 without including the eye.

*Technique for Upper Eyelid.* Former experience has emphasized how dangerous treatment of the upper eyelid may be, since, of the 4 cases previously reported, 3 showed late eye changes and 2 actually suffered from loss of vision; it was shown experimentally that the dose received by the eye from an implant in this situation is much greater than in the case of other sites. With the special technique now evolved, no eye damage at all has been seen in the 5 cases treated, nor in those at the inner or outer canthus with spread to the upper lid.

Adequate protection by filtration would hardly be possible with gamma radiation; it would be impracticable to insert enough metal below the eyelid. It was therefore decided that a trial should be made of distance protection only, since the physical characters of a radiational plane of this type are such that the intensity very rapidly falls off above or below it. Thick contact glasses were employed, and one of these raises the upper lid almost 0.5 cm., thereby reducing the radiation incident on the globe by some 50 per cent. After the implant is completed, the eye is anesthetized with cocaine drops and the glass slipped into position. The whole arrangement is stabilized by stitching the upper lid to the cheek (Fig. 6 and 7). The method appears to cause no great inconvenience to the pa-

Fig. 6. Implant for rodent ulcer of upper eyelid. Contact glass in position, and the lid is stitched to the cheek.

tient, nor is there trouble with the eye (Fig. 8).

Nothing but some congestion in the conjunctiva is seen and this soon passes off; none of the 5 cases has shown any eye damage. In the case of upper lid implants it is not necessary to close the ends of the rectangle unless the lesion is of some size, so only four needles would be employed. Closure can be carried out when it is called for, but may make the operation a little more difficult. The dosage rate naturally falls considerably at the ends of an open rectangle, and care must be taken that the lesion lies well inside; at the extremities the dose delivered would be about half that at the center.

Fig. 7. Contact glass just removed from the eye shown in Figure 6. The staining of the skin here and in Figure 6 is due to the use of proflavine.

CASE DETAILS

Sixty-two patients have been treated by the rapid method between May, 1939 and December, 1942. These include 3 cases of squamous epithelioma affecting skin in the eye region, although the method was not designed for this type of growth. The remainder are basal cell tumors of which 29 were at the eye and the others in various positions about the nose, cheek, or ear (Table II). Biopsy was seldom performed, the nature of most of the cases being obvious clinically.

Fig. 8. Present condition of the patient shown in Figure 6. There are no eye changes.

RESULTS

*Squamous Epithelioma.* The 3 squamous epitheliomas are dealt with separately, since it is by no means clear that the dose given is the ideal one for this histopathological type. One extensive lesion occurring near inner canthus in an aged subject did not appear to respond at all, but a second, treated in 1940 for a lesion at outer canthus involving both lids, received in addition a surface dose of 1,000 r in about twenty-four hours and has done well. The preliminary eye examination revealed some lens opacity in both eyes, together with a chronic atypical glaucoma which has required operative treatment, one eye having been trephined. The third case was treated

Fig. 9. Squamous epithelioma of the eyelids extending from the cheek where the pale area indicates previous use of $CO_2$ snow. The lids are completely rigid through infiltration from the tumor (biopsy performed).

Fig. 10. The patient shown in Figure 9 after treatment by rapid implant. The palpebral fissure is narrowed but the lids now open to some extent.

in 1942 and the lesion, which had begun in the malar region, had received treatment with $CO_2$ snow. This part was healed with dense scarring, but the growth had extended to the lower lid, outer canthus, and upper lid. A rapid implant alone was used to treat these regions, and the parts have healed well; the condition of the eye is excellent though the palpebral fissure is naturally narrow (Fig. 9 and 10).

*Rodent Ulcer.* There were 59 cases of rodent ulcer, situated as indicated in Table II. The lesions are described according to their origins but in a number of cases transgress the primary site, as when an inner canthus growth extends to one or both lids. All present soundly healed areas of skin except 3 where recurrence took place. One of these lesions was on the ala nasi (1941) and no reason is obvious for the failure. The second (1941) was a rodent ulcer in mastoid region involving the ear, and cartilage invasion had occurred so that surgical intervention was likely to be the ultimate outcome; it was successful. The last case presented a very infiltrative lesion of some duration at the inner canthus (1942). It healed well but growth re-appeared late

Table II

| | Epithelioma of Eye Region | Rodent Ulcer | | | | |
|---|---|---|---|---|---|---|
| | | Eye Region | | | | Face Excluding Eye Region |
| | | Upper Lid | Lower Lid | Inner Canthus | Outer Canthus | |
| 1939 | 1 | 1 | 0 | 1 | 1 = 3 | 0 |
| 1940 | 1 | 0 | 1 | 2 | 2 = 5 | 6 |
| 1941 | 0 | 0 | 2 | 3 | 0 = 5 | 7 |
| 1942 | 1 | 4 | 2 | 7 | 3 = 16 | 17 |
| | | 5 | 5 | 13 | 6 = 29 | |
| Totals | 3 | 29 | | | | 30 = 62 |

looking rather as if it had come from below, and it would seem likely that there was deep invasion into the orbit on a scale not obvious clinically. Apart from these 3 failures, mention must be made of 1 upper eyelid case (Fig. 11 and 12). The lesion was extensive and infiltrative, and one tiny nodule of recurrence became obvious a year after treatment. This was promptly excised and the microscopic report indicates that the margins appear adequate.

Fig. 11. Somewhat extensive rodent ulcer of the upper eyelid (biopsy performed).
Fig. 12. The case shown in Figure 11 after treatment. The eyebrow is somewhat epilated.

### IRRADIATION SEQUELAE

*Skin.* The appearance of the skin after treatment is of particular significance in the case of facial lesions, and it is therefore important that the cosmetic results have been good, representing an improvement on the older technique. Where a malignant ulcer has destroyed much tissue, scarring must inevitably result to some extent, and a number of the cases had been quite extensively involved in this way. As a rule, however, there is little to be seen if some slight local pallor is allowed; when this occurs it is rendered less obvious by having no sharply defined margin. The guiding principle in assessing results would seem to be that the changes, if any, should not be conspicuous to the casual observer, and this has been the case except in 6 cases out of the total. Two cases developed small areas of superficial skin slough some time after treatment, but under exceptional circumstances due to undue exposure at work in a shipyard, and as driver of a railway engine. Two others show a good deal of fibrosis but one had previously been given some treatment with $CO_2$ snow; and, finally, 2 show a distinct scarred depression corresponding exactly to the size of the original lesion and not to the area irradiated. Purely irradiation changes of undesirable extent in the skin are probably the result of faulty needle insertion with reference to the skin surface; or to there being very little subcutaneous tissue, as at the bridge of the nose, so that the needles are very near the skin. One or 2 cases show some tendency to formation of blackheads at or near the original site, but this usually happens in patients who do not give the skin reasonable attention. Three of the cases—2 at the inner canthus, and 1 at the upper lid—were recurrent after operation, so already had small scars. No trouble with underlying cartilage or bone has been encountered.

*Eye.* As in the past, these patients undergo ophthalmological examination before treatment and at intervals afterwards, so that the significance of any findings can be more readily assessed in relation to what has been done. Quite a number showed some change or other at the first examina-

tion, including lens opacity, vitreous opacity, vascular changes, choroiditis, and so forth; while several were already troubled by epiphora. One eye had already been largely disorganized by sepsis in a case of extensive and neglected rodent ulcer involving both lids, and in another case both eyes showed some lens opacities with cupping of discs, but no rise of intraocular pressure. It is beyond the scope of these notes to discuss such incidental findings, and only changes seen for the first time after treatment need be referred to. It is worth observing, however, that the case notes do not indicate that any of these conditions were made worse by the treatment, with the possible exception of the septic eye which was already lost as a functional unit.

FIG. 13. Rodent ulcers of face. The inner canthus rodent is beginning to involve the eyelids.
FIG. 14. The case shown in Figure 13 after treatment. There is slight pallor at the inner canthus where the growth was somewhat infiltrative.

Epilation of eyelashes has not occurred to any great extent, and where it has been observed has not been obvious except on close examination. One case has a moderate degree of ectropion. Those patients with epiphora naturally continued to complain of watering of the eyes, but one now thinks that the treated eye is worse; 3 cases developed this symptom after irradiation. Astringent drops or washes containing zinc sulfate may be helpful, and dilatation of the tear duct is occasionally tried. As epiphora may occur when the punctum seems normal in appearance and position, it is evidently the duct which is involved, and it is difficult to see how this can be avoided in a certain proportion of cases, since any form of treatment must cause some fibrosis during healing. If the lesion is in the vicinity of the duct, the lumen is therefore likely to be narrowed or even seriously obstructed. The situation may be summed up by saying that the total number recorded as complaining of new or old watering of the eye or eyes is 8—4 had lesions at the inner canthus, 3 at the lower lid, and 1 on the cheek.

The only abnormalities observed to develop within the eye have been senile changes in the lenses and vessels of both eyes in a patient aged seventy-five. No intraocular damage was seen, even in the upper lid cases. In view of the short time during which the later patients have been observed, it should be stated that any serious ocular complication from irradiation, except cataract, would almost certainly be well developed by now; and that, even in the older series of cases, where larger doses were employed, cataract was not encountered to any extent.

## COMMENT

It is fully realized that the lapse of a few more years would give more weight to what

has been said regarding the efficacy and safety of this rapid implantation method, but the results have been uniform enough to make it appear worth while recording what has already been accomplished. The method is now in regular use for appropriate cases, and these comprise basal cell lesions anywhere, but especially in awkward sites with difficult contours, such as are met with most often around the eye, and occasionally about the nose. It is claimed that the method, in the time observed, has been very efficient, and that post-irradiation trouble has been quite unusual in the skin and was not found in the eye apart from some watering. Further, the saving in time is considerable as compared with older implantation methods. I consider that the cosmetic results are especially good; as has been indicated, the site of treatment is often difficult to distinguish and this alone would seem to make the time of thirty hours worth while spending.

One point of special interest to radiotherapists is the adjustment of the dose to suit the altered treatment time. Reduction in time inevitably implied a lower dose, and the problem was to find one high enough to deal with the tumor, yet not too great for the lower tissue tolerance associated with a short exposure. A skin dose of about 3,000 r in thirty hours appears to answer well; it has been effective without causing excessive reaction or post-irradiation stigmata of note, and no doubt the small volume irradiated has helped in this respect. Basal cell carcinoma is usually so radiosensitive as to lend itself admirably to this type of treatment, and it is a matter of interesting speculation how far the idea can be applied to epitheliomas of the squamous type. The 3 cases cited give at least a suggestion that something can be done along such lines.

For more detailed discussion of the action of radiation in the region of the eye and appropriate references the reader is referred to the original paper.[1]

SUMMARY

A method is described whereby basal cell carcinoma can be treated by implantation of radium in the reduced time of thirty hours. It is claimed that this method appears to be both efficacious and safe so far as it has been observed, and that this is particularly true of the more awkwardly situated lesions on the face. Sixty-two cases were treated in the years 1939 to 1942. There were only three failures, two of which might have been expected, and a fourth case required slight extra attention. It is fully realized that the duration of the follow-up is short, but the results appear sufficiently interesting to merit recording.

A new technique has been evolved for dealing with tumors of the upper eyelid in order to eliminate damage to the eye.

No ocular damage has been encountered in any of the cases described.

I have pleasure in acknowledging the assistance of Professor A. J. Ballantyne, and later of Professor Brownlow Riddell, and their assistants, in examining these cases at the Eye Department, Glasgow Western Infirmary; Professor Lowenstein, at present attached to the Department, kindly supplied the contact glasses. The physical calculations were originally made for me by our physicist, Dr. John Thomson, and after his departure for war duties, by Dr. Walter McFarlane, who is also responsible for the isodose curves. The Visiting Staff has been most helpful in providing ward and theater facilities.

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# EDITORIALS

## ELECTRONICS AND POST-WAR RADIOLOGY

THE Allied war effort owes no little part of its success to the contributions of the science of electronics. Although most of the developments which have occurred in this field remain cloaked in secrecy for reasons of security, it is evident that electronic devices have played and will continue to play a decisive rôle in the solution of many military and naval problems.

The peace-time applications of electronics promise to be no less spectacular than the military. Indeed many imaginative minds envisage an almost incredible future for the science in industrial, agricultural and domestic pursuits. Instruments with which the hazards of aviation will be enormously reduced, new control devices to facilitate our daily routine and rapid advances in television and communications equipment are but a few of the many developments which even the conservative foresee.

Electronic engineering also will have a far-reaching influence on the science of roentgenology. This relationship is a subtle one for the development of the roentgen tube constitutes one of the first practical applications of electronic research.

In medical roentgenology several electronic developments seem imminent. One is the grid-controlled roentgen tube. This device is similar to present-day models but includes in addition to the anode and cathode an interposed electrode having a grid-like structure. This additional element permits increased efficiency in tube operation and also provides a simple means whereby target size may be regulated.

Another electronic device which may prove useful is the photoelectric timing mechanism. This instrument completely automatizes the roentgen procedure so that a technician is required merely to place the subject before the roentgen machine and to close the exposure switch. Time-wasting measurements of anatomical thickness and adjustments of equipment are unnecessary. By its inherent design, the mechanism terminates roentgen exposure at the instant when a film has received the quantity of radiation required for correct exposure. Excellent uniformity of roentgenographic quality thereby is assured. The photoelectric timing mechanism consists essentially of a multiplier phototube with an overlying fluorescent screen and a condenser-thyratron-relay system. The phototube occupies a position immediately below the center of the cassette and records the relative intensity of the roentgen radiation reaching the film. The response of the phototube is integrated by the condenser-thyratron-relay system and the exposure terminated by the opening of the relay's contacts when a certain quantity of radiation has been delivered to the film.

At this writing, grid-controlled roentgen tubes and photoelectric timing mechanisms appear quite practical. They constitute, however, relatively minor contributions. Of much greater significance is the possible development of equipment whereby fluorescent images may be amplified. It must be admitted that the perfection of such devices seems unlikely in the immediate future, but their potentialities are so spectacular as to arouse immediate interest.

From the earliest days of roentgenology, fluoroscopy has remained at a stage analogous to that occupied by the crystal-set in radio. The usefulness of the method has been enormously limited by the low visual

acuity which an observer possesses when working at the low levels of illumination which exist under fluoroscopic conditions. Accordingly most roentgen procedures are conducted with roentgenography, even though this process introduces many technical and clinical disadvantages. It has long been recognized that the limitations of fluoroscopy would be effectively overcome if fluorescent images could be amplified several thousand times so that the illumination of the screen approached the brightness of the usual roentgenographic viewbox. Under these conditions visual acuity is high and pathological processes then could be visualized in multiple projections with the same clarity as that provided by roentgenography. Furthermore, dark adaptation of the operator would no longer be required; indeed fluoroscopic examinations could be conducted in normally lighted rooms, thus permitting the use of roentgen methods in surgery. The use of sufficient amplification would also allow a considerable reduction in the intensity of the exposing radiation. Radiation hazards thereby would be largely eliminated. With fluorescent amplification, roentgenographic procedure would be tremendously simplified for if roentgenograms should be desired it would be necessary merely to photograph the fluorescent screen. Thus powerful roentgen equipment would seldom be required.

Several methods whereby fluorescent amplification may be accomplished have been proposed. One suggests the use of television equipment including the usual iconoscope (television camera), vacuum tube amplifier and kinescope (television projector). The sensitivity of present-day iconoscopes is so low, however, that the amplified image is obscured by extraneous random "noise" generated in the amplifier. Television developments which have occurred during the war may markedly alter this situation but it seems unlikely that such methods will solve the problem of fluorescent amplification. Another method proposed by Langmuir suggests the use of an electronic image tube. This device, schematically illustrated in Figure 1, consists of a cylindrical glass envelope including a fluorescent surface backed by a photoelectric layer at one end of the tube and another fluorescent surface at the other. Along the axis of the tube are cylindrical

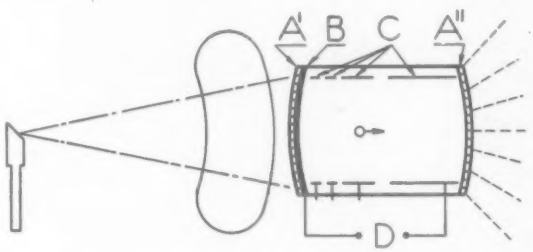


Fig. 1. Simplified schematic diagram of Langmuir image tube. *A'*, *A"*, fluorescent surfaces; *B*, photoelectric surface; *C*, cylindrical electrodes; *D*, high voltage, d.c. source.

electrodes which serve to focus the electronic image. When roentgen rays impinge on the first fluorescent surface, *A'*, the roentgen image is converted to a light image which in turn is converted to an electronic image by the adjacent photoelectric layer, *B*. If a high voltage electrostatic field is applied in the long axis of the tube, the electronic image will be projected on the second fluorescent surface, *A"*, there to be reconverted to a light image. The gain in brightness of the second surface over that of the first will depend on the efficiency of the photoelectric layer, the voltage applied to the tube and the types of fluorescent materials employed. It has been estimated that image tubes may be constructed having an amplification between 10 and 100 times. Although this is a step in the right direction, it is hardly sufficient to fulfill the needs of fluoroscopy.

Another device, the electron multipactor tube suggested by Farnsworth, may provide the eventual solution to the problem. This instrument, illustrated in Figure 2, is similar to the Langmuir image tube but also includes a second photoelectric layer, *B"*, applied to the fluorescent surface, *A"*, at the viewing end of the tube. Furthermore a high frequency rather than a d.c. electro-

static field is employed. As in the simple image tube, a roentgen image is converted to an electronic image at the first fluorescent-photoelectric interface, $A'$, $B'$. This electronic image is projected upon the distal

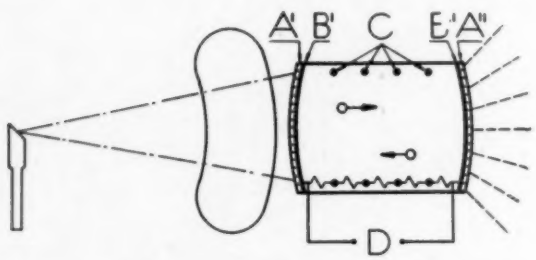


Fig. 2. Simplified schematic diagram of Farnsworth multipactor tube. $A'$, $A''$, fluorescent surfaces; $B'$, $B''$, photoelectric surfaces; $C$, guard-wire electrodes; $D$, high frequency, high voltage source.

end of the tube by the electrostatic field where it first encounters the second photoelectric layer, $B''$, and then the underlying fluorescent surface, $A''$, where it is reconverted to a light image. When an electron impinges on a photoelectric surface it causes the ejection of several other electrons by secondary emission. This effect is analogous to that which occurs when a droplet falls in a pool of water. The interaction of the droplet at the surface of the pool causes several small droplets to be thrown into the air. If the frequency of the electrostatic field is such that the field reverses just at the instant when the original photoelectrons impinge on the second photoelectric layer, $B''$, the electrons produced by secondary emission will be swept back to the first photoelectric surface, $B'$, there to cause the ejection of additional secondary electrons. This process may be continued indefinitely and if at each electronic impact several secondary electrons are produced, the original photoelectric image may be amplified many thousands of times after a few trajectories.

The foregoing description of the principles of a multipactor is a gross simplification. Actually the operation of the device is extremely complicated and many difficulties, several of which appear almost insurmountable, must be overcome before the tube will constitute a practical method of fluorescent amplification. Indeed the instrument at present is little more than an academic curiosity.

Considerable effort will be expended in the post-war era to explore the multipactor's intriguing possibilities. Investigations will also be conducted in other directions, and although it is not possible to predict when fluorescent amplication will become a practical reality, it may be sooner than some of the more pessimistic workers believe.

Russell H. Morgan

# ADOLPH HARTUNG
## 1883-1944

ADOLPH HARTUNG, a member of the American Roentgen Ray Society since 1912, died on May 29, 1944, of coronary stenosis. He was Professor of Radiology in the University of Illinois College of Medicine from 1925 on, where from 1909 he had been instructor. He was a charter member of the Chicago Roentgen Society and was its president for two terms; a fellow of the American College of Radiology, a member of the Radiological Society of North America, and a diplomate of the American Board of Radiology.

Dr. Hartung was born February 26,

1883, in Gotha, Germany. When he was fifteen months old his family moved to Milwaukee, where he attended grade school and high school, after which they moved to Chicago. He became interested in the roentgen ray about 1900, as a demonstrator and salesman, and he demonstrated the rays at the Louisiana Purchase Exposition at St. Louis in 1904. In 1908 he received the degree of Doctor of Medicine from the College of Physicians and Surgeons in Chicago, later the Medical School of the University of Illinois, and had won election to Alpha Omega Alpha. He worked his way through school by serving as a pharmacist's apprentice, and while he had never attended a pharmacy class, he passed the examination qualifying him as a licensed pharmacist.

His early interest in radiology led him after a short period in general practice to resume that activity, and he was successively radiologist to the Alexian Brothers, Grant, Cook County, and University of Illinois Research and Educational Hospitals, He was a genial and informal person, ever the student in both his reading and writing. For several months before his death he knew that he had coronary disease but he chose to continue at work except for occasional short periods of being confined to the hospital; he could not give up to invalidism.

In 1919 Dr. Hartung was married to Miss Clara Henrici, who survives him, with two daughters, Hertha and Annette.

T. J. Wachowski

# SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

*Items for this section solicited promptly after the events to which they refer.*

## MEETINGS OF ROENTGEN SOCIETIES*

### United States of America

**American Roentgen Ray Society**
*Secretary*, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: 1945, to be announced.

**American College of Radiology**
*Secretary*, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill.

**Section on Radiology, American Medical Association**
*Secretary*, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio.

**Arkansas Radiological Society**
*Secretary*, Dr. J. S. Wilson, Mack Wilson Hospital, Monticello, Ark. Meets every three months and also at time and place of State Medical Association.

**Radiological Society of North America**
*Secretary*, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: 1945, to be announced.

**Radiological Section, Baltimore Medical Society**
*Secretary*, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

**Section on Radiology, California Medical Association**
*Secretary*, Dr. Earl R. Miller, University of California Hospital, San Francisco, Calif.

**Radiological Section, Connecticut Medical Society**
*Secretary*, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

**Section on Radiology, Illinois State Medical Society**
*Secretary*, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

**Radiological Section, Los Angeles County Medical Association**
*Secretary*, Dr. Roy W. Johnson, 1407 S. Hope St., Los Angeles, Calif. Meets on second Wednesday of each month at the County Society Building.

**Radiological Section, Southern Medical Association**
*Secretary*, Dr. Roy G. Giles, Temple, Texas.

**Brooklyn Roentgen Ray Society**
*Secretary*, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N.Y. Meets monthly on fourth Tuesday, October to April.

**Buffalo Radiological Society**
*Secretary*, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months.

**Chicago Roentgen Society**
*Secretary*, Dr. F. H. Squire, 1754 W. Congress St., Chicago 12, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

**Cincinnati Radiological Society**
*Secretary*, Dr. Samuel Brown, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

**Cleveland Radiological Society**
*Secretary*, Dr. D. D. Brannan, 11311 Shaker Blvd., Cleveland 4, Ohio. Meets at 6:30 P.M. at Allerton Hotel on fourth Monday each month, October to April, inclusive.

**Dallas-Fort Worth Roentgen Study Club**
*Secretary*, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meetings held in Dallas on odd months and in Fort Worth on even months, on third Monday, at 7:30 P.M.

**Denver Radiological Club**
*Secretary*, Dr. Edward J. Meister, 366 Metropolitan Bldg., Denver, Colo. Meets third Friday of each month at Denver Athletic Club.

**Detroit Roentgen Ray and Radium Society**
*Secretary*, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

**Florida Radiological Society**
*Acting Secretary*, Dr. Walter A. Weed, 204 Exchange Bldg., Orlando, Fla. Meetings in May and November.

**Georgia Radiological Society**
*Secretary*, Dr. James J. Clark, 478 Peachtree St., Atlanta, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

**Radiological Society of Kansas City**
*Secretary*, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month at a place designated by the president.

**Illinois Radiological Society**
*Secretary*, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

**Indiana Roentgen Society**
*Secretary*, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meeting held the second Sunday in May annually.

**Kentucky Radiological Society**
*Secretary*, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

**Long Island Radiological Society**
*Secretary*, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

**Louisiana Radiological Society**
*Secretary*, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

**Michigan Association of Roentgenologists**
*Secretary*, Dr. E. M. Shebesta, 1429 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

**Milwaukee Roentgen Ray Society**
*Secretary*, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

**Minnesota Radiological Society**
*Secretary*, Dr. Annette T. Stenstrom, 1218 Medical Arts Bldg., Minneapolis, Minn. One meeting a year at time of Minnesota State Medical Association.

**Nebraska Radiological Society**
*Secretary*, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

**New England Roentgen Ray Society**
*Secretary*, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

**Radiological Society of New Jersey**
*Secretary*, Dr. H. R. Brindle, 501 Grand Ave., Asbury Pk. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

**New York Roentgen Society**
*Secretary*, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

**North Carolina Roentgen Ray Society**
*Secretary*, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

North Dakota Radiological Society
*Secretary*, Dr. L. A. Nash, St. John's Hospital, Fargo. Meetings held by announcement.

Central New York Roentgen Ray Society
*Secretary*, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

Ohio Radiological Society
*Secretary*, Dr. Henry Snow, 1061 Reibold Bldg., Dayton, Ohio.
Meets at time and place of annual meeting of Ohio State Medical Association.

Pacific Roentgen Society
*Secretary*, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
*Secretary*, Dr. L. E. Wurster, 416 Pine St., Williamsport.

Philadelphia Roentgen Ray Society
*Secretary*, Dr. R. P. Barden, University Hospital, Meetings first Thursday of each month from October to May inclusive at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

Pittsburgh Roentgen Society
*Secretary*, Dr. L. M. J. Freedman, 4800 Friendship Ave. Meets second Wednesday each month, 4:30 P.M., October to June, Pittsburgh Academy of Medicine.

Rochester Roentgen Ray Society, Rochester, N. Y.
*Secretary*, Dr. Murray P. George, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
*Secretary* Dr. A.M. Popma, 220 N. First St., Boise, Idaho.

St. Louis Society of Radiologists
*Secretary*, Dr. E. W. Spinzig, 2646 Potomac, St. Louis, Mo. Meets fourth Wednesday of each month, except June, July, August, and September, at a place designated by the president.

San Diego Roentgen Society
*Secretary*, Dr. Henry L. Jaffe, Naval Hospital, Balboa Park, San Diego, Calif. Meets monthly on first Wednesday at dinner.

San Francisco Radiological Society
*Secretary*, Dr. Martha Mottram, 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six months of year at Toland Hall, University of California Hospital, second six months at Lane Hall, Stanford University Hospital.

Shreveport Radiological Club
*Secretary*, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Carolina X-Ray Society
*Secretary*, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
*Secretary*, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
*Secretary*, Dr. Asa E. Seeds, Baylor Hospital, Dallas, Texas. Next annual meeting, Temple, Texas, January 17, 1945.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
*Secretary*, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
*Secretary*, Dr. E. L. Flanagan, 116 E. Franklin St., Richmond, Va. Meets annually in October.

Washington State Radiological Society
*Secretary*, Dr. Thomas Carlile, 1115 Terry St., Seattle. Meets fourth Monday each month, October through May, College Club, Seattle.

X-ray Study Club of San Francisco
*Secretary*, Dr. J. M. Robinson, University of California Hospital. Meets monthly in evening on third Thursday.

### Cuba

Sociedad de Radiología y Fisioterapia de Cuba
*President*, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

### British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Medical Members' meeting held monthly on third Friday at 2:30 P.M. and Ordinary Meeting at same time on following Saturday, October to May, 32 Welbeck St., London, W.1.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month at 4:45 P.M. at the Royal Society of Medicine 1, Wimpole St., London, W. 1.

Faculty of Radiologists
*Secretary*, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1 England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
*Secretary*, Dr. H. M. Cutler, 139 Macquarie St., Sydney. New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
*Secretary*, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

Canadian Association of Radiologists
*Secretary*, Dr. A. D. Irvine, 540 Tegler Bldg., Edmonton, Alberta.

Section of Radiology, Canadian Medical Association
*Secretary*, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Radiological Section, New Zealand British Medical Association
*Secretary*, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

### South America

Sociedad Argentina de Radiologia
*Secretary*, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

### Continental Europe

Sociedad Espanola de Radiologia y Electrologia
*Secretary*, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
*Secretary* for French language, Dr. A. Grosjean La Chaux de Fonds.
*Secretary* for German language, Dr. Scheurer, Molzgasse Biel. Meets annually in different cities.

Societatea Romana de Radiologie si Electrologie
*Secretary*, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad: USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
*Secretaries*, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
*Secretaries*, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
*Secretaries*, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

# A HISTORICAL NOTE ON ROENTGENOLOGIC LITERATURE

Having recently come into possession of Volume 1, No. 1 (Fig. 1) of the *American X-Ray Journal* which made its appearance forty-seven years ago, it seems worth while to publish some notice of this ancestor of the American Journal of Roentgenology and Radium Therapy.

The announcement of the advent of the *American X-Ray Journal*, written by Heber Robarts, M.D., Editor, contains many points which are sound even at this time (Fig. 2). The *American X-Ray Journal* was the second published in English and the first published in America. It was preceded by the *Archives of Skiagraphy* which was published in London in 1896.

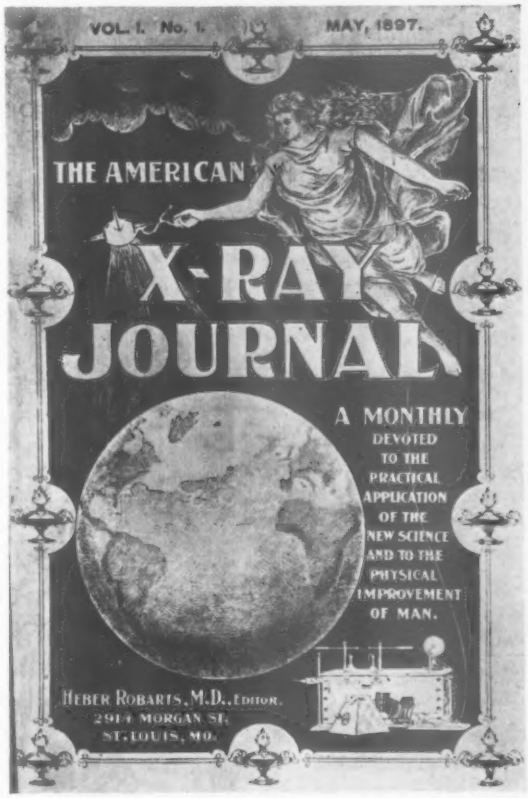
VOL. I. No. 1. MAY, 1897.
THE AMERICAN
X-RAY JOURNAL
A MONTHLY
DEVOTED TO THE PRACTICAL APPLICATION OF THE NEW SCIENCE AND TO THE PHYSICAL IMPROVEMENT OF MAN.
HEBER ROBARTS, M.D., EDITOR.
2914 MORGAN ST.
ST. LOUIS, MO.

Fig. 1. (*right*) Cover of the *American X-Ray Journal.*

Fig. 2. (*below*) Announcement of the appearance of the *American X-Ray Journal.*

THE AMERICAN

# X-RAY JOURNAL.

A Monthly Journal devoted to Practical X-Ray Work and Allied Arts and Sciences.

VOL. I. ST. LOUIS, MO., MAY, 1897. No. 1.

THE AMERICAN X-RAY JOURNAL,
PUBLISHED MONTHLY.

YEARLY SUBSCRIPTION RATES—IN ADVANCE.

United States, Canada, and Mexico ..... $1 00
Single copies ..... 10
Foreign Countries ..... 1 25
Single copies ..... 15

HEBER ROBARTS, M. D., Editor,
2914 Morgan Street, St. Louis, Mo.

## ANNOUNCEMENT.

No apology is considered necessary for undertaking the publication of the American X-Ray Journal, the "first born" of its kind, and a journal in line with human thought and the practical needs of man.

Fifteen months have passed since the Wurzburg professor first announced the discovery of the x-ray, and no great has the interest become that every item pertaining to the new science is grasped by the public press with avidity. The claims made by Professor Roentgen were received at the time with commingled incredulity and amusement, and are even at this date not properly appreciated by some professional reading people.

The medical profession have a record for amplifying, pruning, and utilizing new facts for the benefit of humanity and themselves, but in this instance there are financial, mechanical, and technical difficulties which must be surmounted by them before the x-rays can be practically applied. Again, inefficient apparatuses are everywhere used by exhibitors and forced upon the attention of doctors. It is on account of these facts that physicians do not readily adopt the new science, notwithstanding the public clamor for its use.

The ease and certainty of diagnosing some surgical affections has advanced more in the past twelve months than any previous hundred years. In the first experiments with the x-rays it was thought possible to photograph only the bones of the hands, and this only after long exposure, while examinations with the fluoroscope were considered too tedious and impracticable. But the usefulness of the x-rays has so rapidly extended that no bone of the human body has escaped successful photography, and the bones have been examined directly with the fluoroscope.

Successful work is being done also in diagnosing cases of cancer, tumors, appendicitis, gall stones, renal and urinary stones, enostosis of the cranium and blood clots, in addition to the more common cases of fracture, diseased joints, and the locating of foreign substances in any portion of the body. In the fluoroscope the heart is observed and studied in its movements, the diaphragm is outlined and seen to rise and fall with respiration, and the visceral organs can be studied.

The application of the x-rays has been used with success in certain cases of the blind, in nervous twitching, tremulous agitations of the hands and body, and also the annoying rotatory movements of the eye-ball (nystagmus). Other avenues of inquiry have been opened for the x-ray application, notably cold abscesses within the body, degenerative germinal affections, especially consumptive abscess and the early diagnosis of this disease, and also the practical use of the x-ray in dentistry.



It is the design of this journal to give to readers and thinkers a faithful resume of all x-ray work done in any portion of the globe. The editor's personal experience with the x-rays for practical purposes, together with seventeen years of medical and surgical experience, filling many official medical positions, and traveling largely in search of medical facts, renders the task of imparting x-ray information more appropriate for those who read and think. It is the intention of the promoters of this journal to give to the world only truthful results, with full credit to the experimenter in all its relations to the new science.

This field of inquiry must have associated with it practical and useful adjuncts. The most essential which shall occupy space are medico-legal jurisprudence, the therapy of electro-medical science, preventive medicine, hygiene, dentistry, and collateral branches.

We shall favor correspondence with pro or con criticism so long as it deals with the subject matter of the journal.

No advertisements shall appear in this journal that savor of quackery, deception, or fraud.

Medical and scientific publications reflect the sittings of individual thought, and the press gives the practical side and vitalizes the facts. Their work must be equally commended and personal gratitude acknowledged.

The conduct of this journal shall not be arrogant, defiant, or bigoted, but it will have the courage of conviction to press forward the truth as we understand the truth. It will be ethical, as the throbbings of every breast should be, regardless of any written code devised by man for another's guide. There will be no personal venom, as we hold no animus against any man, but false principles will be attacked with the vigor of our ability. This is a pioneer journal of x-ray work. We are not imitators. We are casting our hopes among the needs and wants of man. We expect encouragement.

While it can not be expected nor desired that we shall escape just criticism, add it may be commonly, yet our aim shall be to improve each coming journal, encouraged as we are in the faith and usefulness of our mission.

HEBER ROBARTS, M. D., Editor.

## A PREMIUM OFFER.

The subscription price of the American X-Ray Journal is $1.00 per year. While this price is low when the character of the journal is taken into consideration, we have made arrangements by which we can offer additional inducements to subscribers. We will send the Journal for one year and the following named books pertaining to x-rays at the prices annexed: "A B C of the X-Rays" (price, 75 cents) and the Journal for $1.40.

"The X-Ray or Photography of the Invisible" (price, 75 cents) and the Journal for $1.40.

Both of the above books and the Journal for $1.80.

"Roentgen Rays and Phenomena of the Anode and Cathode" (price, $1.50) and the Journal for $2.20.

These three books are richly illustrated, beautifully printed on coated papers, and handsomely bound in cloth.

The great numberless questions coming to us through the mail seeking information in regard to the x-ray have become too voluminous and too important for individual reply. We have concluded, therefore, to make a catechismal text of these inquiries, and annex to each a brief answer or definition. Calculating from what we have now, and the probable result from general extended requests for further questions as a basis for judgment, we feel confident of being able to continue

The editor of the *American X-Ray Journal* was both the first and second president of the American Roentgen Ray Society founded in 1900. The office of the journal and of its editor was located at 2914 Morgan Street (now Delmar Boulevard) St. Louis, Missouri (Fig. 3). The photograph of this house indicates the descent of a neighborhood from one of relative affluence to one of abject poverty.

Fig. 3. Home and office of Heber Robarts, M.D., Editor of the *American X-Ray Journal*. This house is located in the center of what is now the "blighted" district of St. Louis.

Few files of the *American X-Ray Journal* are in existence and many, if not most, radiologists are unaware of the existence of this publication important in its day. The great number of present day radiological publications obscures the significance of these early efforts.

From the meager beginnings at the time of Roentgen's discovery, November 8, 1895, there is now a world wide roentgenologic literature. The Army Medical Library in Washington lists thirty-five such journals.

Sherwood Moore

## CANCER TEACHING DAY

On October 17, 1944, a Cancer Teaching Day was held at the Herman M. Biggs Memorial Hospital, Ithaca, New York, under the auspices of the Medical Society of the County of Tompkins, the Medical Society of the State of New York, and the Division of Cancer Control of the New York State Department of Health. The following papers were presented at the afternoon session: "Carcinoma of the Colon," by Dr. John H. Garlock, New York City; "Bone Tumors," by Dr. John J. Morton, Rochester, New York. At the evening session a paper was presented by Dr. Andrew H. Dowdy, Rochester, New York, on "Epithelioma of the Skin," and one by Dr. Frank E. Adair, New York City, entitled "Carcinoma of the Breast."

## OHIO RADIOLOGICAL SOCIETY

At the annual meeting of the Ohio Radiological Society the following officers were elected: *President*, Dr. Clarence E. Hufford, Cleveland; *Vice-President*, Dr. H. G. Reineke, Cincinnati; *Secretary-Treasurer*, Dr. Henry Snow, Dayton. *Members of the Executive Council:* Dr. Ralph Holmes, Chillicothe and Dr. John Newton, Cleveland.

## PITTSBURGH ROENTGEN SOCIETY

At the meeting of the Pittsburgh Roentgen Society held on May 10, 1944, the following officers were elected for the coming year: *President*, Dr. William J. McGregor, Pittsburgh; *Vice-President*, Dr. James R. Gemmill, Monesson; *Secretary-Treasurer*, Dr. Lester M. J. Freedman, Pittsburgh.

## ERRATUM

In the paper by J. J. McCort, C. N. Davidson and H. J. Walton entitled "Determination of the placental site in bleeding during the last trimester of pregnancy," in the August, 1944, issue of this Journal, Vol. 52, pp. 128–135, the summary 5(*c*) on page 134 should read: "Widening of sacral promontory-fetal head distance when the placenta is implanted upon the posterior wall."

# BOOK REVIEWS

*Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.*

MEDICAL PHYSICS. Otto Glasser, Ph.D., Editor-in-Chief, Head, Department of Biophysics, Cleveland Clinic Foundation; Professor of Biophysics, Frank E. Bunts Educational Institute; Consulting Biophysicist, University Hospitals of Cleveland, Cleveland, Ohio. With 23 Associate Editors and numerous contributors. Paper. Price, $18.00. Pp. 1744, with many illustrations. Chicago: The Year Book Publishers, Inc., 1944.

This is a compendium of information useful for the investigator in biological and medical sciences and informative to those engaged in specialized or general medical practice. The title of the book fails to express the catholicity of its scope, unless there be agreed that as a definition for the term "physics" there be adopted the earlier connotation of the Hellenic φύσικχ namely the science and principles of that existing materially in nature, including chemistry and biology. Only under such a broadened definition can it be understood why subjects such as ecology, chlorophyll, odor, hydrogymnastics, and gait, are included with roentgenography, electron diffraction, encephalography, centrifugation, electron microscopy, vacuum technic, and osmosis in living systems.

The foreword states a three-fold objective of the editor-in-chief: (1) an encyclopedia of all aspects of medical physics; (2) a textbook to serve students, and (3) a working instrument containing data for actual applications to medicine. The volume is indeed encyclopedic: it appears to be entirely unsuited for a textbook; it should be of aid in practice to those with adequate knowledge.

The general index is extensive; a classified table of contents supplementing the alphabetical table of contents doubtless reflects the selections of the 23 associate editors in the subgroupings of like number. There is an occasional strange inclusion in a sub-group as for instance "microphotography" under the heading "Anatomy," but in general, one can locate without too much difficulty one or more expositions with bibliographic citations on almost anything that he might include under the title of this book, and much that is no less interesting and pertinent because it is unexpected. This is indeed a stimulating agglomeration of technical information and explanations of a melange of interesting and utilizable topics, most of which belong clearly in the realm of Medical Physics.

JOHN W. M. BUNKER

SYMPOSIUM ON RADIOGRAPHY. Held at the Thirty-ninth Annual Meeting, Atlantic City, N. J., June 30–July 1, 1936, and Forty-fifth Annual Meeting, Atlantic City, N. J., June 23, 1942, of the American Society for Testing Materials. Cloth. Price, $4.00. Pp. 256, with 177 illustrations. Philadelphia: American Society for Testing Materials, 1943.

The medical radiologist who is interested in what is going on outside his immediate field will find this book worth while. Part of it, having to do with the roentgenography of massive cast or welded structures by the use of megavolt equipment is real entertainment for those who like to know what "the other fellow" is doing and can do, even though it is not applicable to the reader's own field. Other parts of the book, having to do with highly developed techniques in microradiography, for example, are applicable to the medical field as are some of the studies of light alloys wherein fine detail is brought out in spite of a range of thickness and density far beyond those encountered in the human body.

An interesting sidelight which makes a story in itself is the modern use of filters in roentgenography. Years ago, much work was done on the use of filters in medical roentgenography but with the development of the Bucky diaphragm nearly all of this work fell into the discard. The Bucky, however, is of little use in industrial work, while modern roentgen powerplants make it possible to use thin filters of high atomic number (also a modern development) to great advantage.

There is a chapter on protection, by Lauriston S. Taylor, of real practical use to anyone planning a new installation.

K. E. CORRIGAN

ROENTGENOGRAPHIC TECHNIQUE: A MANUAL FOR PHYSICIANS, STUDENTS AND TECHNICIANS. By Darmon Artelle Rhinehart, A.M., M.D., F.A.C.R., Professor of Roentgenology and Applied Anatomy, School of Medicine, University of Arkansas; Roentgenologist to St. Vincent's Infirmary, Missouri Pacific Hospital, and the Arkansas Children's Hospital, Little Rock, Arkansas, etc. Third edition, thoroughly revised. Cloth. Price, $5.00. Pp. 471, with 201 illustrations. Philadelphia: Lea & Febiger, 1943.

As the author states in his preface, this is a thoroughly revised text of his manual on roentgenographic technique. Although the general plan of the book has remained unchanged, many recent advances made in this field have been added. The essential physics of roentgenography are covered quite adequately and outlined in such a manner as to be readily understood and absorbed by the beginner. Many students entering a training course in roentgen technology as high school graduates without additional college experience are having their major difficulty with this aspect of the course. Yet it is very important for them to master the fundamental physics since the knowledge of what is happening "behind the controls" distinguishes the true technician from a mere robot. There are a few minor flaws in the book —as, for instance, the right part of Figure 191— however, they do not detract in any way from its value as a guide for those for whom it was written. The fact that it appears now in its third edition speaks for itself.

ERNST A. POHLE

ABRIDGED SCIENTIFIC PUBLICATIONS FROM THE KODAK RESEARCH LABORATORIES. Paper. Pp. 391, with numerous illustrations. Rochester, New York: Eastman Kodak Company, 1943.

This is a compilation of sixty papers published during 1942 by members of the Kodak Research Staff. The major portion of the papers are concerned with advanced organic chemistry. Also included are: a paper (No. 840, page 163) by D. L. MacAdam, "Visual sensitivities to color differences in daylight," of considerable interest to anyone studying color response of the eye; a "general interest" paper on color photography (No. 832, page 121) by C. E. K. Mees; and a number of papers on the physics of solutions.

K. E. CORRIGAN

INFECTIONS OF THE PERITONEUM. By Bernhard Steinberg, M.D., Director of Toledo Hospital Institute of Medical Research; Past Fellow of the National Research Council; Former Crile Research Fellow, Western Reserve University. With a Foreword by Frederick A. Coller, M.S., M.D., Professor of Surgery, University of Michigan Medical School; Director, Department of Surgery, University Hospital, Ann Arbor, Michigan. Cloth. Price, $8.00. Pp. 455, with 44 illustrations. New York: Paul B. Hoeber, Inc., 1944.

This is a refreshing and instructive book by a man who has spent eighteen years working on the problem of peritoneal infections. He has made many important contributions to our present day knowledge of the condition. Anyone, surgeon and practitioner alike, concerned with the diagnosis and treatment of peritonitis in its many phases will profit by a careful consideration of the material presented. The author presents new concepts regarding developmental mechanism, diagnosis and treatment. The pathology and its associated disturbance of physiology and chemistry are stressed. The bibliography is exhaustive. Conflicting opinions involving therapy are commented upon and evaluated. The major portion of the book is clinical in nature, including case studies to illustrate the material presented. I know of no comparable volume on the subject.

LLOYD W. STEVENS

# DEPARTMENT OF TECHNIQUE

*Department Editor:* Robert B. Taft, M.D., B.S., M.A., 103 Rutledge Ave. Charleston, S. C.

## A DEVICE FOR MEASUREMENT OF HEART SIZE IN MINIATURE ROENTGENOGRAMS AND A SUBSTITUTE FOR TELEROENTGENOGRAPHY AND ORTHODIASCOPY

*By* RICHARD GUBNER, M.D., *and* HARRY E. UNGERLEIDER, M.D.
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MINIATURE roentgenograms of the chest, either 35 mm. or 4×5 inch size, made by the fluororoentgenographic technique (photography of the fluoroscopic screen), are now generally employed in surveys in the armed forces, institutions and industry. Measurement of the size of the heart cannot be accomplished directly because of the reduced size of the cardiac shadow, and also because miniature films are exposed at shortened focal distance, with consequent appreciable projection magnification.

The simple procedure illustrated in Figures 1 and 2 makes possible the exact measurement of the size of the heart, so that early enlargement may be recognized employing accepted standards for the transverse diameter and frontal cardiac area.* A lead scale with markings at 0.5 cm. intervals is placed alongside the patient in the plane of the anterior axillary line. The scale is recorded on the roentgenogram when the chest exposure is made. The photograph of the scale on the miniature film serves as a reference for measurement of the cardiac shadow, and the cardiac diameters may be read off directly on the scale employing a caliper. Since the scale is suspended in the anterior axillary line in the same plane as the contours of the heart, the projection magnification of the heart and the scale are practically identical.

* Ungerleider, H. E., and Gubner, R. Evaluation of heart size measurements. *Am. Heart J.*, 1942, *24*, 494–510.

This method is equally applicable for the conventional 14×17 inch roentgenogram and makes unnecessary the use of teleroentgenographic (2 meter) distance, which requires high power equipment for desirable short exposures. In roentgenoscopy the orthodiascopic method may be employed to eliminate projection magnification, which is considerable because of the proximity of the tube to the fluoroscopic

Fig. 1. A lead scale suspended parallel to the cassette in the plane of the anterior axillary line is recorded on the roentgenogram. Projection magnification is of the same order as the heart, and reduction in miniature roentgenograms is likewise identical. The scale recorded in the roentgenogram serves as reference for cardiac measurement.

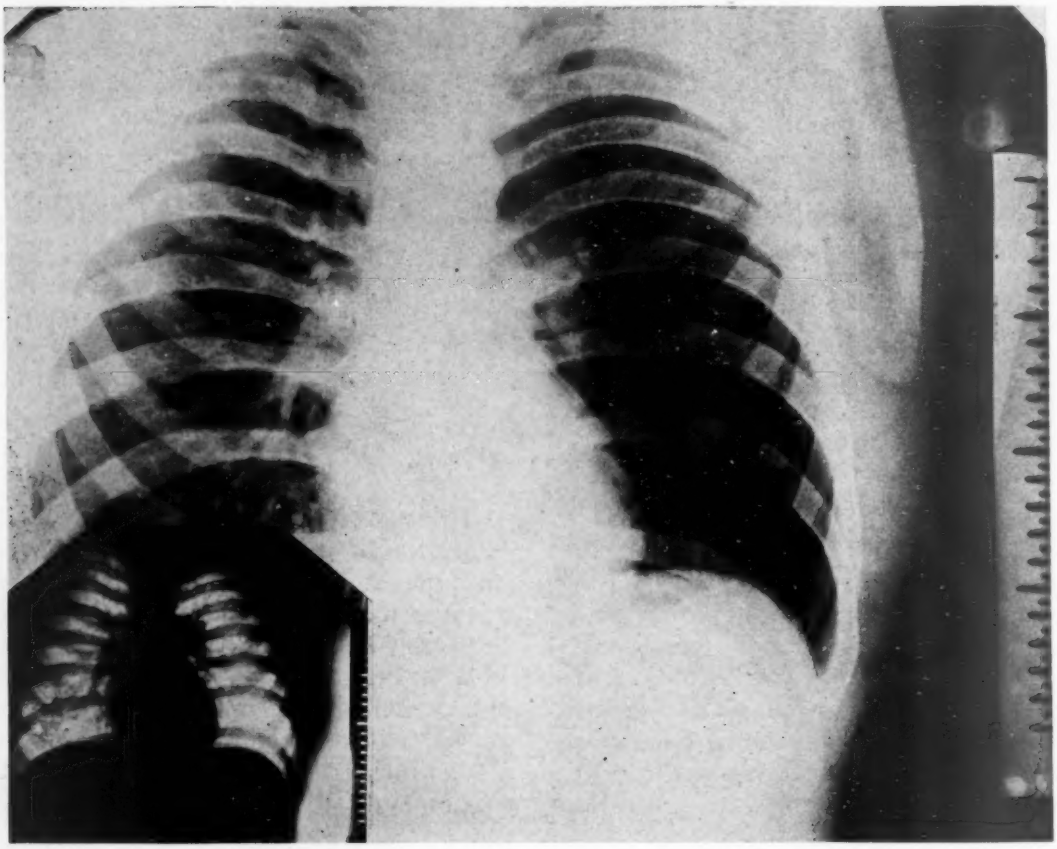

FIG. 2. Scale with 0.5 cm. markings recorded on 14×17 inch roentgenogram as shown in Figure 1. Insert shows fluororoentgenogram of same subject recorded on 35 mm. miniature film at 3 ft. distance. Transverse diameter is same with both techniques (12.0 cm. in 14×17 inch roentgenogram, 11.9 cm. in 35 mm. miniature film).

screen. Orthodiascopy requires a special attachment, permitting the roentgen tube to be moved independently of the screen, the central ray (indicated by a lead marker) being used to trace the outline of the heart. The orthodiascopic technique requires training and exact application for precision, since there is a large subjective element. The use of the lead scale, as indicated in Figure 1, permits accurate measurement of the size of the heart on ordinary roentgenoscopic examination without the need of specialized apparatus as required in orthodiascopy.

The scale may be suspended in proper position in several ways. It may be mounted to slide on two horizontal bars attached to the cassette or screen by suction cups (Fig. 1), or it may be attached in the anterior axillary line with adhesive tape, suspended by a shoulder strap, or mounted on a floor stand. It is important that the scale be parallel to the cassette to avoid foreshortening of the image, and that it be placed correctly in the anterior axillary line.

## SUMMARY

A method is described for the accurate measurement of the size of the heart in miniature roentgenograms. This method serves also to obviate the need of teleroentgenography and orthodiascopy for elimination of projection magnification in the roentgenogram and roentgenoscopic image.

# RADIUM CONTAMINATION OF ROENTGEN FILMS

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THE finding of unexplained black spots on roentgen films was very annoying during normal times but during the present film shortage it is a serious matter. In medical roentgenograms the spots are generally recognizable as artefacts but in industrial roentgenography they are easily confused with defects in castings and weldings. Figure 1 shows such a spot, which was the largest encountered, though a large number of slightly smaller ones have been found. These spots have been proved to be the result of small quantities of radium salts incorporated in the cardboard of which the film box is made.

I first noticed these spots in March, 1942, on the films of one of the leading companies. All of the films in a box showed these spots and in the same location but the films in one side of the box showed the spots to be of much greater density. Many of the films were usable but others were so badly marked that additional roentgenograms had to be made with films from another source.

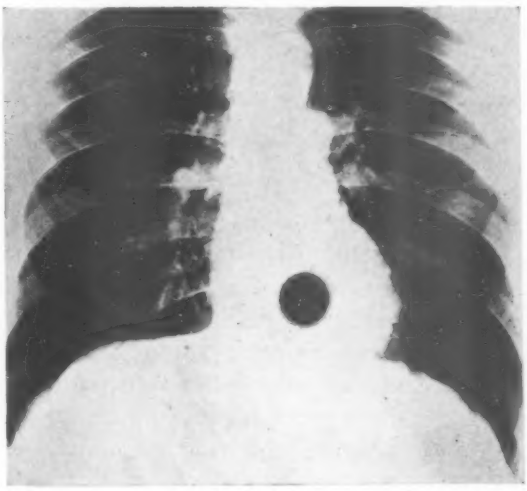

FIG. 1. Film spot due to small particle of radium salt incorporated in the cardboard box containing the films.

In 1939, a radiologist had the misfortune to break a 10 milligram tube of radium sulfate which resulted in many of the articles in his office being contaminated with fine particles of radium salt. I was asked to make tests on the materials and found that the cassettes had been sprinkled with minute particles which gave a blackened spot on the roentgen film after they had been in close contact for several days.

FIG. 2. A film developed without exposure serves as a guide to the placing of the Geiger-Müller counter tube on the exact part of the box containing the radium particle.

The appearance of the spots on the roentgen films recently seen were so similar to those caused by the minute particles of radium that I undertook to determine if these spots could be caused by similar materials. As a result, the boxes in question were torn up and new films in light-tight containers were clamped against the cardboard for several days at a time. Following standard development, the characteristic spots appeared on the new films.

As many as thirty such spots have been seen on a single 14×17 inch film but most of them are comparatively small, though the one shown in Figures 1 and 2 is of such intensity that most of the films in the half gross box had to be discarded.

Occasionally a spot will have the shape of a dumbbell; however, this is not the result of two radioactive particles but of the films having been at rest for several months and then the box receiving a sudden jolt causing the films to shift to a slightly different position.

FIG. 3. Combination autoradiograph and photograph enlarged 14 diameters to show the exact location of the spot in the section for microscopic study.

The possibility that these boxes had been contaminated by radium dust in my office is eliminated by the fact that the same conditions were encountered in several boxes at a hospital where there is no radium.

The final proof that these spots are caused by radioactive material is obtained from the Geiger-Müller counter which shows the presence of gamma radiation. As shown in Figure 2, the spot is first localized by superimposing the film on the box, then the counter tube is placed as close as possible to it. Repeated counts, as well as controls on the boxes which showed no spots, demonstrate the undeniable effect of radioactive material.

Precision measurements on a radioactive particle of this size offer many difficulties but measurements made in different ways all showed a radium equivalent of approximately 0.0005 microgram in the particle shown in Figures 3 and 4.

The manufacturers were most generous in their replacement of defective films but admitted their complete inability to determine the cause. One manufacturer eliminated the difficulty by obtaining the cardboard boxes from another source. Recently, having found more of these spots, I attempted to determine the type of offending material and to learn a method by which it may be eliminated before the films are put up in the boxes.

A known location in a box having been proved radioactive by the Geiger-Müller counter, exact localization was accomplished by placing films on each side of the card, then cutting out a small circle (about 9 mm.) and testing this. Most of these tests took an exposure of about twenty-four hours but when thinner sections were made of the circle of cardboard, an exposure of an hour was sufficient. A strongly radioactive spot was finally located in the middle of a section approximately 0.48 mm. in thickness. As hand-cutting could not be done further, this piece was embedded in paraffin and cut with a microtome into sections 20 microns thick. These sections were then laid out on slides, covered with cellophane, and strips of film placed on them. A five minute exposure showed that one section contained most of the material, another a small amount and a third showed faint trace. The problem was then to determine the exact location of the radioactive spot in the section, as microscopic examination showed only miscellaneous material. The section was placed in a printing frame with roentgen film on the bottom and, after a five minute exposure, light was flashed on the frame which gave a photographic silhouette of the section. This photograph-

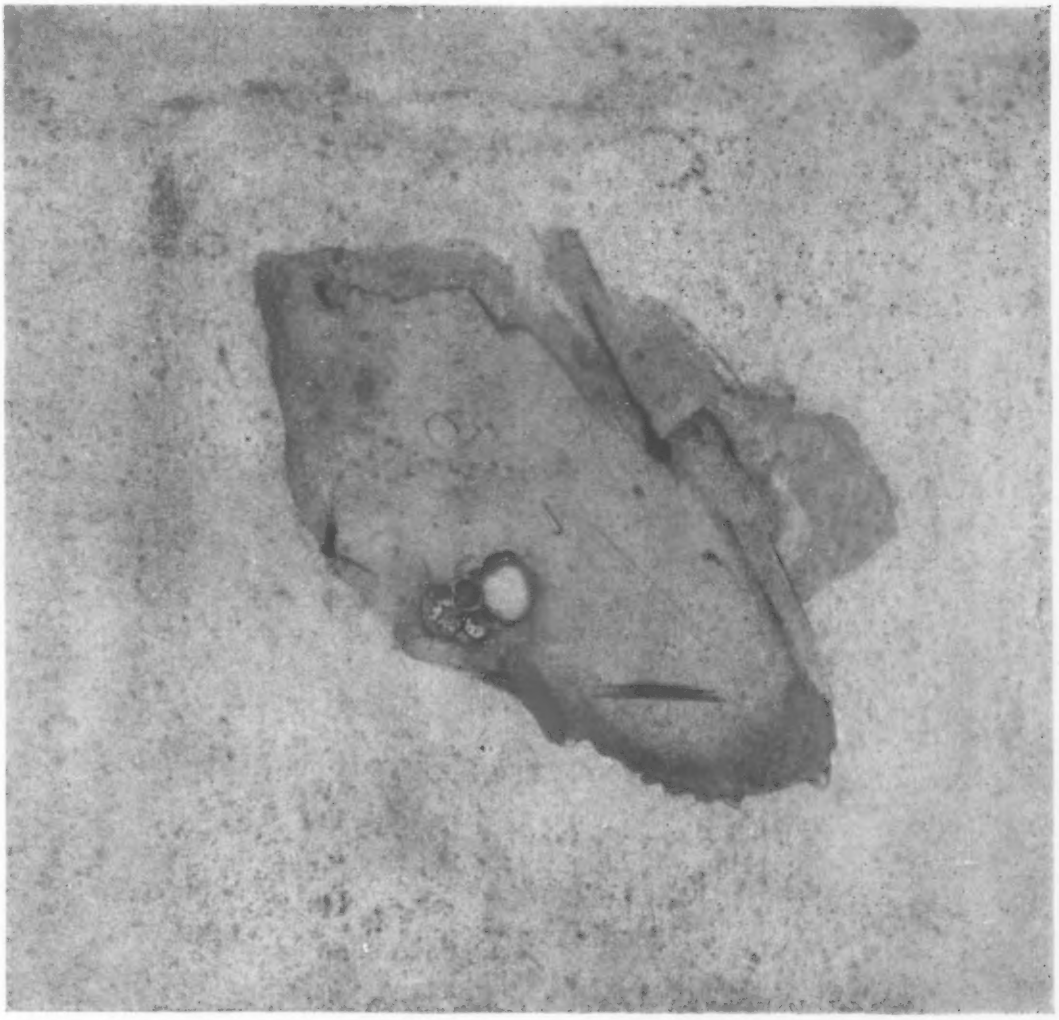

Fig. 4. Colored drawing showing remarkable contrast of the radioactive spot against the other material of the cardboard, as seen by near ultraviolet light. Fourteen diameter enlargement.

radiograph, enlarged about 14 diameters, is shown in Figure 3 and permits exact localization. In this spot a small pile of pale green crystals could be seen. The appearance and gamma-ray activity was similar to radium luminous paint. It was far more active than uranium oxide, or carnotite.

Subsequently, a much simpler method of location has been found; that is, observation under near ultraviolet radiation from the $BH_4$ lamp. Figure 4 is a colored drawing of this slide under a 14 power microscope. The intensity of color is no exaggeration; in fact, this spot stands out so clearly that without any magnification it can easily be seen at a distance of 10 feet. Nothing else has been found in the card that fluoresces appreciably.

How this substance gets into the paper mash will probably remain a mystery but inspection of the mash under ultraviolet light is so simple that the manufacturer can inspect many square yards of it at a glance, and possibly reach the source of contamination. To the radiologist who encounters this condition, the suggestion is offered that films be immediately removed from the box in order to prevent further blackening.

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## ADDENDUM

It was stated above that one manufacturer eliminated the difficulty by obtaining cardboard boxes from a different source but since this paper was written, numerous spots have been found showing that the second source was contaminated also.

Information recently received from the Dupont Company is that in the dial painting industry the brushes are now wiped on tissue paper instead of in workers' mouths, as was done in the old days. The tissues frequently find their way in with other waste paper and subsequently become cardboard boxes.

For the above reason, it is doubtful if occasional spots of this kind will ever be completely eliminated.

Furthermore, the film manufacturers claim that as they have no control over the manufacture of cardboard they are unable to carry out the idea of having the mash inspected by black light.

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# ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

## ROENTGEN AND RADIUM THERAPY

Windeyer, B. W. Radiation reactions. *Brit. J. Radiol.*, Aug., 1942, *15*, 236–237.

The basal cells of the skin are more sensitive to irradiation than the prickle cells and squamous cells. The prickle and squamous cells are not renewed when the basal cells are destroyed by irradiation and the skin becomes thinner until finally there is desquamation down to the basement membrane.

The two chief points in the treatment of radiation reactions is the control of infection and the elimination of trauma. The tannic method of treatment of thermal burns has not proved as effective for radiation burns. Another method of treating thermal burns is that of irrigation with electrolytic sodium hypochlorite in the Stannard oiled silk envelope. This method is also very comfortable for radiation reactions and brings about rapid healing and a minimum of scarring. It is effective even in post-irradiation buccal necrosis which is one of the most difficult post-irradiation conditions to treat.

Connective tissue reactions vary greatly even when the same dose of irradiation is used. Two cases of carcinoma of the larynx may be treated with the same dose and one will progress normally while increasing edema of the arytenoids may develop in the other. In the latter results are apt to be very unsatisfactory no matter what changes in technique are adopted. The cause of this difference is not known.—*Audrey G. Morgan.*

Ellis, F. Volume dosage in deep x-ray therapy. The estimation of volume dosage in deep x-ray therapy for clinical purposes. Part II. The correlation of biological effects with volume dose. *Brit. J. Radiol.*, July, 1942, *15*, 194–201.

A study is made of the relationship between volume dose and biological effects. Tables and graphs are given showing the effect of varying volume doses on the blood picture. Accurate correlation is impossible, however, as the graphs vary greatly in form, and quantitative and even qualitative changes in the leukocyte picture are not uniform for given volume doses. The number of cases examined was limited, however, and it is possible that with larger numbers of cases more uniform results would be obtained.

Experiments are also described in the use of histaminase and ascorbic acid in the treatment of irradiation sickness. So far the author's experience indicates that histaminase is more effective for this purpose than ascorbic acid.—*Audrey G. Morgan.*

Farmer, F. T. A direct-reading radon meter for clinical purposes. *Brit. J. Radiol.*, Nov., 1942, *15*, 318–319.

Radium, on account of its cost, must be measured very accurately. But radon seeds degenerate quickly and therefore the need in measurement is rather for quickness and simplicity with a sufficient degree of accuracy for clinical purposes.

An instrument for such measurement is described and illustrated with a photograph and a diagram. It consists of an ionization chamber and an electrometer valve system so that any source of gamma rays applied to the chamber can be read directly on the scale of a meter in the anode circuit. By controlling the voltages supplying the valve carefully it can be kept constant enough and it is not necessary to use substitution of a standard potential source as in more accurate measurements. It is operated from batteries, one of about 100 volts supplying the anode and chamber, and a 2-volt accumulator feeding the filament. Both are small and readily portable. Calibration is by means of radium tubes of known strength. It is accurate to within 2 to 3 per cent which is sufficient for practical purposes.—*Audrey G. Morgan.*

Ellis, Frank. Tolerance dosage in radiotherapy with 200 kV x rays. *Brit. J. Radiol.*, Dec., 1942, *15*, 348–350.

From published work and his own clinical experience the author concludes that there is such a thing as resistance on the part of the tissues to malignant disease. The optimum dose is the dose that will just allow the normal tissues to return to normal after irradiation, as that will inflict the maximum damage on the

malignant cells and enable tissue resistance to be utilized to the maximum degree. The tolerance dose means the dose that is tolerated by connective tissue, which is the tissue responsible for resistance and repair. Except in certain regions, such as the nervous system and bone, this is similar to the tolerance dose of the skin. Therefore the tolerance dose for the skin represents the optimum dose for treating malignant tumors. It is more important to preserve the resistance of the connective tissue bed of the tumor than it is to give a definite dose to each malignant cell.

A table is given showing a system of tolerance dosage produced at 200,000 volts constant potential and used mostly at 40 cm. distance with a filter of 1 mm. copper and 1 mm. aluminum. By continued accurate observation and the collaboration of other radiotherapists he hopes that corrected tables of this kind can be worked out. He also gives doses for inflammation and sterilization.—*Audrey G. Morgan.*

Wilson, C. W. The combination of radiation fields in deep x-ray therapy. *Brit. J. Radiol.*, Dec., 1942, *15*, 355–359.

Much of the success of radiation therapy depends on the distribution of radiant energy by suitable arrangements of the beams based essentially on the dose contours of the beams. Desjardins says that the anatomical arrangement of the treatment is more important than the quantity of radiation given to any one field.

Any focus of disease should be irradiated with a dose which is as uniform as possible over the whole site and it should be as large a fraction as possible of the maximum dose given to any of the skin areas through which the beams pass. If the distribution of the irradiation is satisfactory it lowers the amount that need be given to any skin area. The dose delivered to diseased tissues should not be exceeded by the dose to any normal tissue within the irradiated area.

Illustrative dose contours are given for the treatment of cancers of the larynx and lung. Irradiation should be given from two opposite lateral fields and in some cases from a third posterior field. In the cases illustrated the factors were: 200 kv. (peak) (Villard circuit), 30 ma., focus skin distance 50 cm.; Thoraeus filter; half-value layer 1.63 mm. copper; fields 6×8 and 10×8 cm. The conditions of dose and scatter used in treatment should be as nearly as possible equivalent to those under which the dose contours were originally determined. This method involves more work than the usual one but this is much more than compensated for by the better results obtained.—*Audrey G. Morgan.*

Williams, I. G. Very high voltage x-ray therapy (supervoltage). *Brit. J. Radiol.*, Dec., 1942, *15*, 360–364.

In 1938 and 1939 the author visited roentgen clinics in the United States, and in this article he examines the claims made in regard to the superiority of high voltages (400 to 1,200 kilovolts) as compared with 200 to 250 kv. treatment. Depth dosage curves are given which show that between 400 kv. and 900 kv. backscatter increases by 6 per cent and depth dose by 5 per cent for a field 10×10 cm. in size. The principal factor that limits increase of dosage is the mucosa rather than the skin as in 200 kv. therapy. It has not yet been proved that the higher voltage rays have a different biological effect than the lower ones. Radiation sickness is less severe with the higher voltages than the lower. It is easier to maintain body weight on account of decreased nausea and vomiting. Within therapeutic doses the higher voltage radiation does not injure the blood-forming organs. There are better palliative results in advanced malignancies of the skin, uterus and prostate and in large clinics where a great variety of malignant tumors are treated the range of usefulness of roentgen therapy will probably be increased by the use of high voltage rays.

A bibliography is given of the work of the American radiologists and physicists consulted. —*Audrey G. Morgan.*

MacCarty, William C., and Leddy, Eugene T. Roentgen treatment of inoperable ulcerating carcinoma of the breast. *Radiology*, Dec., 1942, *39*, 711–714.

One of the most distressing features in cases of inoperable carcinoma of the breast is ulceration. A study of case histories showed that the development of this stage is usually due to neglect of early treatment. From 1925 to 1940 inclusive the authors treated 98 patients with primary inoperable ulcerating carcinoma of the breast in the Section of Therapeutic Radiology at the Mayo Clinic. Forty of these patients had not gone for treatment before coming to the

clinic. The remaining 58 had not gone to a physician until they had had symptoms for an average period of 15.5 months. Of these 25 were given sound advice by their family physicians while the other 33 were given unsound advice, such as treatment with salves, pastes, lights, electricity, etc.

While any treatment of these cases is necessarily only palliative, the authors have found marked alleviation from roentgen treatment by the multiple converging beam technique. In the majority of cases they use 130 kv. (constant potential), 6 ma., 40 cm. target-skin distance and 6 mm. aluminum filtration. The anterior part of the thorax on the affected side is divided into four or six sectors, each sector centered over the tumor. The central rays are directed toward the center of the sector. If there are metastatic lesions they are treated as required. A dose of 500 to 600 r, measured in air, is given to each sector at one sitting. Usually treatment is given to one area or perhaps two daily; the full course may require from four to eleven treatment days. The series is repeated in a month and again after another month and later treatment given as indicated.

At the end of 1940, 43 of the patients were dead; there was no follow-up report from 24 but they were also probably dead. Twenty-four patients were living and said that they were definitely improved, while only 7 said that they were worse. There was the greatest number of improvements in the patients who had three or more courses of treatment, the fewest in those who had only one. After one course of treatment the average duration of life from the first treatment was slightly less than seven months while after three courses of treatment it was slightly more than a year and a half.—*Audrey G. Morgan.*

Lederman, M., and Mayneord, W. V. The radium treatment of cancer of the vagina. *Brit. J. Radiol.*, Nov., 1942, *15*, 307–312.

Primary cancer of the vagina constitutes only about 1 to 2 per cent of tumors of the female genital tract. Metastatic cancer is much more frequent. Treatment of these cancers has not heretofore been very successful because of their rarity and the lack of experience that any physician could acquire, because of the vascularity of the region and the advanced stage of the disease when the case is generally seen.

The best method of treatment is the local application of radium followed by teleradium or high voltage roentgen treatment to the lymphatic areas of the pelvic and inguinal regions. In radium treatment the size and shape of the applicators must be adapted to the case, the applicators must be fastened firmly in position and the surrounding normal tissues must be adequately protected. A detailed description is given of the making and application of a urethral tube and vaginal applicator for use in this treatment and curves given showing the distribution of radiation around the tube and applicator. As the urethral tube is used to stabilize the applicator the patient must be anesthetized and to avoid the risk of infecting the bladder if the treatment is frequently repeated, treatment should be given two or three times, separated by intervals of two or three weeks. Sometimes in addition to this treatment groups of needles must be implanted at the base of the bladder. The radium treatment is followed by teleradium or high voltage roentgen treatment to clear up what is left of the primary disease and to irradiate the lymphatic areas.—*Audrey G. Morgan.*

Schmitz, Herbert E., Sheehan, John F., and Towne, Janet. The effect of preoperative irradiation on adenocarcinoma of the uterus. *Am. J. Obst. & Gynec.*, March, 1943, *45*, 377–390.

The technique for the treatment of carcinoma of the uterine fundus by combined roentgen and radium therapy as employed at the Mercy Hospital Institute of Radiation Therapy is as follows: All patients are curetted and a Y-capsule containing 50 mg. of radium element in each arm is immediately inserted into the uterine cavity. The capsule is removed after 2,000 mg-hr. This dose is repeated on the eighth and sixteenth days giving a total radium dosage of 6,000 mg-hr. On the days that the radium is not in the uterus the patient receives roentgen therapy. The dose attained within the pelvis after twenty-eight days is 4,000 roentgens, with backscatter.

A group of 77 proved cases of adenocarcinoma of the uterine fundus has been studied. Eleven patients receiving preoperative irradiation were hysterectomized. Five of the uteri adequately treated (as outlined above) were free of carcinoma. Serial blocks of 4 of these 5 uteri failed to reveal residual carcinoma. The remaining 6 patients considered as inadequately treated all had active carcinoma remaining in the uterus.

Twenty-seven cases, irradiated but not hysterectomized, added further evidence as demonstrated by curettage or follow-up that adequate irradiation in clinical Group I or II carcinoma of the fundus has a definite value. Although the authors do not advocate their treatment as a substitute for surgery in patients who are good surgical risks, they feel that their plan of preoperative irradiation should be carried on until sufficient case records are on hand to determine whether the five year survival rate is greater than in cases treated by surgery and postoperative irradiation.—*Mary Frances Vastine.*

Rongy, A. J., and Seley, A. D. Radium therapy in benign uterine bleeding; study based on 350 cases. *Am. J. Obst. & Gynec.*, March, 1943, *45*, 390–401.

Broadly conceived, surgery is but an admission of the shortcomings of medical science. The greater the progress of the science of medicine, the less will be the need for surgical intervention. Intrauterine irradiation, used in properly indicated cases, will reduce the operative incidence in patients suffering from uterine bleeding, with or without fibroids, in about 35 per cent. The authors feel that 1,800 mg-hr. is the appropriate dose for women aged forty years or older. They insert 25 mg. in the uterus to be left seventy-two hours. They conclude:

(1) Uterine bleeding can be cured by curettage and intrauterine insertion of radium in properly selected cases.

(2) In 285, or 81 per cent of the patients studied, the bleeding was accompanied by fibroids; in 65, or 19 per cent, no fibroids were present.

(3) Complete involution of the tumor took place in 81.4 per cent of the cases and partial involution in 16.8 per cent. In 5 patients, the tumor was not affected by the radium.

(4) Radium is contraindicated in cases in which the uterus is enlarged to more than fourteen weeks' pregnancy. It should not be used when a submucous fibroid is suspected nor is its use advisable in subperitoneal or broad ligament fibroids.

(5) It is dangerous to use radium in patients who give a history of having had a pelvic infection.

(6) The menopausal syndrome is not accentuated by radium.

(7) Leukorrheal discharge is increased for a period of six to seven weeks in many cases.

(8) Sexual relationship is less likely to be disturbed following the use of radium than with surgery. The libido is definitely not affected.

(9) Curettage and intrauterine irradiation can be safely utilized in at least 35 per cent of patients suffering from uterine bleeding. It should replace abdominal hysterectomy in 25 per cent of cases and vaginal hysterectomy in 40 per cent.

(10) Curettage and radium therapy should be performed by gynecologists, not by radiologists.—*Mary Frances Vastine.*

Buschke, F., and Cantril, S. T. Roentgen therapy of carcinoma of the urinary bladder; analysis of fifty-two patients treated with 800 kv. roentgentherapy. *J. Urol.*, Oct., 1942, *48*, 368–383.

This report is a summary of 52 cases of carcinoma of the urinary bladder treated over a six year period with 800 kv. roentgen therapy. Thirty of these cases were treated with a current of 10 ma., a filter of 4.5 mm. of lead, skin-target distance of 70 cm., and an intensity of 60 r per minute. The remaining cases were treated at a skin-target distance of 100 cm. with an intensity of 25 r per minute. The areas treated were essentially a central suprapubic, a central posterior, left and right sacrals and an occasional perineal field which was treated with 200 kv. and 2 mm. of copper filtration.

Five of the 52 cases were free from disease cystoscopically after five years and 2 other cases for more than one year. The dosage varied from 6,000 r, measured in air, delivered to two fields to 17,000 r delivered to four fields. The treatment period varied from thirty to sixty days.

The authors give the following reasons for failure to control the majority of cases in this series: invasion of the muscular bladder wall by the tumor; technical errors in treatment such as limiting the field to too small an area, or too intensive or insufficient treatment; attempting to treat cases in which the disease process was too extensive; poor general condition of the patient, resulting in inadequate dosage or spacing of dosage over too long a period of time, and, finally, complications from previous therapy such as breaking down of a suprapubic scar. The authors give case reports illustrating these various reasons for unsatisfactory results.

They conclude that all papillary tumors of the bladder which are of a type tending to recur

or which have recurred once following fulguration should receive roentgen therapy as the procedure of choice at once, if at all. In cases of infiltrating tumors they feel that resection is the procedure of choice, if feasible. Contraindications to intensive roentgen therapy include poor general condition of the patient, inadequate bladder drainage, inadequate bladder capacity, and the presence of marked secondary infection.—*R. M. Harvey.*

Randall, Lawrence M., and Buie, Louis A. Factitial proctitis. *Am. J. Obst. & Gynec.*, March, 1943, *45*, 505–512.

"Factitial proctitis" is a term used to designate the changes sometimes incurred in the wall of the rectum when the pelvic viscera are treated by radium or roentgen rays. (The term "factitial" is defined in Dorland's Dictionary as "produced by artificial means; unintentionally produced.") Usually this lesion appears on the anterior wall of the rectum but in severe cases all walls may be involved. It varies in severity from mild inflammation of the rectal mucosa to complete dissolution of a portion of the rectovaginal septum.

*Pathology and Diagnosis.* Factitial proctitis, not associated with formation of ulcer, cannot be detected by palpation. The factitial ulcer averages from 1 to 3 cm. in diameter and is usually single. The inflammation and ulceration have a tendency to heal and if the carcinoma does not terminate the patient's life the lesion usually will undergo resolution.

*Symptoms.* In 88 cases studied, bleeding was the most frequent symptom. Other complaints in order of frequency were: frequent desire to go to stool, liquid stools, pain in the rectum, mucous discharges, and constipation. The average time that elapsed between the initial course of treatment and appearance of symptoms was ten months.

*Results of Examination.* The average location of the factitial proctitis was 9 cm. above the dentate margin. In 6 of the 88 cases, the involvement was diffuse and in the remainder it was circumscribed and located on the anterior wall of the rectum. In 25 cases reduction in the size of the rectal lumen was noted. There were 3 rectovaginal fistulas and they were 5 to 6 cm. above the dentate margin.

*Results.* Of the 30 patients who were followed from eight months to thirteen years, 25 noted marked improvement in the rectal symptoms after the acute stage. Most of them experienced occasional bleeding from the rectum, some a tendency to constipation and one stated that the stool was reduced in size.

*Treatment.* Healing will usually take place providing the patient survives the malignancy for a sufficient time. In cases in which strictures develop obstruction will not occur unless extension of the cancer has been the cause of this stricture. Considering the very small percentage of patients treated with irradiation whose normal tissues sustain significant damage, and the gradual improvement in results following such treatment, it seems that factitial proctitis and ulceration (and the occasional rectovaginal fistula) must be accepted as risks that the patient should assume when such treatment is undertaken.—*Mary Frances Vastine.*

## MISCELLANEOUS

Bradford, Donald. A belated review. *Brit. J. Radiol.*, Aug., 1942, *15*, 224–227.

This is a review of a book published in 1896, soon after the discovery of x rays by Roentgen in December, 1895. It was not written by a roentgenologist but by a schoolteacher, Arthur Thornton, M.A., who was a teacher in one of the provincial grammar schools. It shows the great interest aroused in all scientifically minded people by the discovery of the rays. Curiously enough, many of the modern developments in roentgenology were forecast at that early date and the early theories discussed in the book are strikingly like those generally accepted today. For example the ionization measurement of intensity is generally thought to be quite modern but Thornton describes a method which established the property of ionization. At that time biological effects were not realized, however, and there was no reference to any precautions being necessary in handling the rays. Several pages of the book are reproduced. —*Audrey G. Morgan.*

Barclay, A. E. The passing of the Cambridge diploma. *Brit. J. Radiol.*, Dec., 1942, *15*, 351–354.

The *British Medical Journal* for November 29, 1941, carried a notice that the courses leading to the Diploma of Medical Radiology and Electrology given at Cambridge would be discontinued and no further diplomas would be granted after October 31, 1942. This article reviews the early history of radiology when it was considered largely a branch of photography

and useful in medicine only in diagnosing fractures and localizing foreign bodies up to the present time. At the beginning of World War I roentgenological knowledge and practice were not very far advanced and the war brought about chaotic conditions. An army x-ray committee was set up and the leading radiologists worked untiringly to establish better conditions. After the war the need for more thorough training in this branch was recognized and discussion of the matter led finally to the establishment in March, 1919, of the course for the Diploma, the first part to be the study of physics and elementary radiology to be given in Cambridge and the second part to be clinical work in London. Credit is given to this course and the devoted work of the leading radiologists in teaching for much of the phenomenal progress in radiology that has been made since that time. —*Audrey C. Morgan.*

Teall, C. G. A regional radiodiagnostic service. *Brit. J. Radiol.*, Oct., 1942, *15*, 289–292.

In post-war planning the author thinks there should be an effort to bring about better cooperation between the voluntary and municipal hospitals. Both these classes of hospitals have heretofore treated only the poorer classes of the population while those better provided for were obliged to depend on nursing homes, not nearly so well equipped. It is now proposed to raise the income limit for National Health Insurance to 420 pounds sterling per annum which will embrace about 90 per cent of the population of the country. With hospital service available to so large a percentage of the population it will hardly be possible for a radiologist to support private equipment.

A suggestion is made that the country be divided into regions and these into divisions. Each region will have a key hospital and the divisions smaller hospitals serving the communities. Each regional hospital will have a radiological staff, the junior members of which can be sent out to the smaller hospitals when occasion requires. The most expensive and elaborate equipment will also be installed in the regional hospitals and simpler equipment will suffice for the smaller hospitals. There will be a transportable van equipment which can be carried to the homes when necessary. The Public Health Service will provide for mass examination in tuberculosis. In this way all the needs of all the communities in the country will be provided for, whereas at present there are many small communities that have no radiological service at all.—*Audrey G. Morgan.*

Jefferson, Geoffrey. The problems of post-war reconstruction in radiology; the future of the specialties. *Brit. J. Radiol.*, Oct., 1942, *15*, 283–285.

Hospitals grew up from the charitable motive of caring for the sick and wounded and as a result were adapted entirely to the needs of general medicine and surgery. But as science has developed, a number of specialties have arisen each of which requires time, space and money. The hospital of the future will probably be a Hospital Center with a number of specialist departments around a nucleus of general medicine and surgery, the latter to be used chiefly for the training of medical students. The student must get a balanced training without overemphasis on any one specialty. Yet as a matter of fact at the present time most physicians and surgeons are more or less specialists. For instance the general surgeon is for the most part an abdominal specialist and the student is led to believe that gallstones and stomach diseases are the chief things to be considered in surgery. In the properly balanced hospital of the future more time and space will be alloted the specialist and less to the general physician and surgeon.—*Audrey G. Morgan.*

Hodgson, H. K. Graham. Radiological education of the future. *Brit. J. Radiol.*, Oct., 1942, *15*, 292–293.

The author believes that the present nine months course required for a diploma in radiology is far too short and that too much of it is devoted to physics. He thinks that a two years course should be required and that the first six months should be devoted entirely to refresher courses in anatomy, physiology, pathology and clinical methods. The next twelve months should be spent in a roentgen-ray department in the study of radiology and roentgenography, separate courses being given for the students of diagnosis and therapeutics. During the final six months he should correlate what he has learned of roentgen appearances with the clinical and pathological facts seen in the operating room, wards and postmortem room. During these six months he would be a clerk or registrar to the roentgen department and act as a liaison officer between the roentgen department and the

other members of the hospital staff. He thinks this would give a higher standard for qualified roentgenologists.—*Audrey G. Morgan.*

Stebbing, G. F. Radiotherapeutic education of the future. *Brit. J. Radiol.*, Oct., 1942, *15*, 294–296.

The Faculty of Radiologists now insists on the candidate for a Fellowship examination spending a year in a hospital appointment to acquire a knowledge of medicine, surgery and pathology. To get an adequate knowledge of the specialties he must work as a member of a team which should include a physician, surgeon, radiodiagnostician, laryngologist, gynecologist, physicist and pathologist. Each member of the team learns from the others. All of them should see the patient and have a first-hand knowledge of the disease.

After qualification he should spend two years doing house appointments at a teaching hospital. During this time he should learn all he can about clinical medicine and pathology and should attend as many postmortems as possible. After this he should spend a further period as a surgical registrar at a teaching hospital or as resident surgical officer in a hospital. He must be able to work equally well with roentgen rays and radium and in the latter work he must be capable of doing minor surgery and doing it well.

After this training in medicine and surgery he should spend a year in taking a course for the diploma in radiology. Radiotherapists and radiodiagnosticians should have separate training as these are quite different fields. After he gets his diploma in radiology he should get a post as assistant in a radiotherapeutic clinic where he can continue to learn radiotherapy and he should have some time to do research work as there is so much research to be done in this field.

This is a long and expensive course and there should be posts in which money can be earned and the developing radiation therapist given the status and responsibilities of other senior members of the staff.

Undergraduates in medicine should not be taught any radiation therapy for in this field as in many others a little knowledge is a dangerous thing. This teaching should be entirely post-graduate. General practitioners of medicine should be taught only the kind of cases that should be sent to the radiotherapeutic center.

There are few radiotherapists now being trained in England and the author suggests that the Director of the Emergency Medical Service in the Ministry of Health should encourage some of the younger surgeons to turn to radiotherapy.—*Audrey G. Morgan.*

Trostler, I. S. Employer is liable in common law for physician's fees for services rendered injured employe. *Radiology*, Feb., 1943, *40*, 191–192.

Industrial commissions in several states have attempted to fix the amount of compensation to be paid physicians or surgeons for treating injured employes. But the Illinois Appellate and Supreme Courts have decided in several cases appealed from lower courts that the industrial commission has no authority or right as between the physician and his patient. The workmen's compensation laws make the employers and employes parties to a contract but the physician is not a party to this contract and has the same right to fix his fees as in other cases. Other states have made similar decisions and the higher courts of no state have upheld the industrial commissions in the matter. Cases are cited in which the decisions and the reasons for them are given at length.—*Audrey G. Morgan.*

McGrigor, D. B. Radiographic stereoscopy. *Brit. J. Radiol.*, Oct., 1942, *15*, 273–281.

Stereoscopic roentgenography is of great advantage in the examination of regions such as the thorax, pelvis and skull where confusing superimposed shadows are placed in their separate planes in the stereoscopic image. But the correct technique for viewing stereograms is not very well understood and errors due to this fact has probably led to neglect of a very valuable method. The routine of making the stereograms is briefly described. The stereograms must be viewed both at the sam etime in such a way that the left eye sees only the one taken from the left tube shift and the right eye only the one taken from the right tube shift. A detailed description is given of the method of setting up the stereograms correctly. If the films are not placed upside down, sideways, or in such a way that the anatomical relations are incongruent, there are only four possible placements and only one of these gives a really correct stereoscopic view. The correct and incorrect combinations are shown by diagrams and ster-

eograms and their probable stereoscopic images by composite photographs.—*Audrey G. Morgan.*

Kerley, Peter. Technique in mass miniature radiography. *Brit. J. Radiol.*, Dec., 1942, *15*, 346–347.

The miniature roentgenogram does not compare in detail with the full-size one and therefore this method is used only for sifting cases of comparatively gross disease. The 5×4 inch film used in the United States does not show any greater detail than the miniature 35 mm. one and therefore the latter is to be preferred on account of cheapness and speed.

On a single posteroanterior view about 0.2 per cent of early tuberculous lesions are overlooked on account of their small size. With both anteroposterior and posteroanterior views they are much more apt to be projected free of rib shadows and detected. A survey with 35 mm. films has shown that with the two views diagnostic accuracy is about the same as that with full-size films. The disadvantage of taking two views is that fewer cases can be examined per hour and there is more wear and tear on the apparatus. A well trained team could probably take two views of 100 cases per hour. This is of no consequence compared with the great advantages of being able to detect early tuberculous lesions on the miniature roentgenogram.—*Audrey G. Morgan.*

Bourke, V. V. A method for the localization of foreign bodies and a new instrument to carry out this method. *Radiology*, Jan., 1943, *40*, 56–61.

A new and more accurate method of localizing foreign bodies is described which is based on the principle of parallax, that is, that shadows of foreign bodies at an equal distance from the roentgen tube move equal distances on the fluoroscopic screen when the tube is shifted.

There are two pieces of apparatus for carrying out the method. The first is a fluoroscopic screen which moves the length of the table and parallel to it. It also moves at right angles to the table and can be raised or lowered any desired distance. The tube beneath the screen and table except when released follows all lateral motions of the screen so that the vertical ray is always centered on the center point of the screen. The second piece of apparatus is a set of calipers, the tips of which can be raised or lowered and a line connecting the tips will always be parallel to the plane of the fluoroscopic screen and table. When the arms are set at zero the tips will be together and in the vertical ray and their shadows will coincide with the center point on the screen. The screen and calipers are adjusted until the tips of the calipers make two indelible marks on the member containing the foreign body. A straight line drawn between these two points will pass through the foreign body while the distance of each mark from the foreign body is known from the readings on the calipers.

There is also an instrument to be used by the surgeon for the interpretation of the roentgen-ray markings and the localization of the foreign body. Any surgeon can adjust it in two minutes.

All the parts of the apparatus are illustrated and their application described in detail. The method is simple and requires no figuring or trigonometry. The measurements are mechanical, being read directly from the scale. The method is rapid, accurate and simple.—*Audrey G. Morgan.*

Schwarzschild, Myron M. A multiple cassette changer for angiocardiography; device for rapid serial radiography. *Radiology*, Jan., 1943, *40*, 72–74.

In angiocardiography a large amount of concentrated dye is rapidly injected into the brachial vein. Roentgenograms of the thorax taken immediately afterward show the course of the contrast medium through the heart and lungs. At present satisfactory results can be obtained only by direct roentgenography, using a 10×12 inch film. In order to obtain roentgenograms showing even one stage of the process a number of exposures, at least six, must be made in a short time.

The author describes and illustrates an improved apparatus for accomplishing this. It consists essentially of three compartments arranged in a straight line—the magazine compartment into which the cassettes are loaded, the exposure compartment in which each film is exposed and the receiver compartment in which they accumulate. The cassettes are stacked in the magazine compartment in front of a pressure block. The patient is positioned and the controls adjusted. The thrust bar is pushed in, pushing a cassette into position in front of the opening. The contrast substance is then injected. On withdrawal of the thrust bar

a pivoted mercroid switch closes the circuit, operating the roentgen ray timer and making an exposure. On the next inward thrust of the bar another cassette is pushed into position and this pushes the previous one into the receiver compartment. A simple timer has been incorporated into the device, so that each film carries a record of the time of its exposure.—*Audrey G. Morgan.*

Bell, A. L. L. X-ray therapy in fluoroscopy. *Radiology*, Feb., 1943, *40*, 139–144.

It has been shown that relatively small doses of roentgen rays produce changes in the chromosomes that may affect the offspring and that the effect may be cumulative, not only during the life of the individual but during successive generations.

Now that fluoroscopes are produced at a price that makes them available to all, many physicians are doing their own roentgen examinations. In one eastern city it was found that practically one practicing physician out of four had a fluoroscope. Many of these fluoroscopes are provided with timers in an attempt to reduce the danger but if the whole of the dose is delivered over the pelvis or the lower abdomen the amount striking the gonads is much greater than if the upper part of the body is irradiated.

In order to determine the amount of radiation to which the patient is subjected in routine examinations, the author made measurements with a fluoroscope equipped with an ionization chamber and connected with a Braestrup irradiometer. Tables are given showing the results which indicate that dangerous doses are often given, especially by untrained personnel or practicing physicians other than roentgenologists. The physician as well as the patient is exposed to danger unless he wears a lead-impregnated apron and gloves.

Fluoroscopic examinations should not be done promiscuously nor should the ovaries or testicles of patient or examiner be exposed unnecessarily.—*Audrey G. Morgan.*

Speert, Harold. Swallowing and gastrointestinal activity in the fetal monkey. *Am. J. Obst. & Gynec.*, Jan., 1943, *45*, 69–82.

Swallowing and gastrointestinal activity have been demonstrated in the fetal monkey by means of serial roentgenograms following the injection of radiopaque substances (usually thorotrast). The injection was made into the amniotic sac at various stages of gestation between 99 and 155 days. The following findings were noted: (1) The rate of swallowing of amniotic fluid increases and the emptying time of the fetal stomach decreases as pregnancy progresses. (2) No evidence exists that there is, normally, defecation in utero. (3) Water is absorbed by the fetal intestine thereby producing a concentration of the intestinal contents. (4) Rebreathing by the maternal animal has no demonstrable effect on the rate of propagation of the intestinal contents of the fetus.—*Mary Frances Vastine.*

Jesser, Joseph H., and de Takats, Gèza. Visualization of the pulmonary artery during its embolic obstruction. *Arch. Surg.*, June, 1941, *42*, 1034–1041.

Contrast visualizations of right heart and pulmonary arteries in dogs, before and after production of massive pulmonary embolism, plus effects of several drugs on the appearance of these structures, are presented. On the basis of these observations, other experimental evidence and experience in emergency treatment of pulmonary embolism clinically the following conclusions are drawn:

(1) Epinephrine is contraindicated in pulmonary embolism because of its tendency to increase the pulmonary hypertension and accelerate failure of the right heart (neosynephrin and digitalis may work similar harm).

(2) Papaverine produces increased pulmonary vascularity and has a bronchodilator effect.

(3) Emergency treatment of pulmonary embolism should consist of administration of oxygen and intravenous injection of atropine and papaverine.—*H. G. Moehring.*